UNITED STATES BANKRUPTCY COURT FOR THE DISTRICT OF DELAWARE

PROOF OF CLAIM

1. Name of Debtor (YOU MUST SELECT ONE AND MAY ONLY SELECT ONE DEBTOR):

[X] Graceway Pharmaceuticals, LLC (11-13036)
[ ] Graceway Pharma Holding Corp. (11-13037)
[ ] Graceway Holdings, LLC (11-13038)
[ ] Chester Valley Holdings, LLC (11-13039)
[ ] Chester Valley Pharmaceuticals, LLC (11-13041)
[ ] Graceway Canada Holdings, Inc. (11-13042)
[ ] Graceway International, Inc. (11-13043)

This form should not be used to assert a claim for an administrative expense arising after the commencement of the case, which should be filed pursuant to 11 U.S.C. § 503. Additionally, this form should not be used to assert a claim under 11 U.S.C. § 503(b)(9), which should be filed pursuant to the 503(b)(9) Administration Order, entered on October 17, 2011 [Docket No. 122].

2. Name of Creditor (the person or other entity to whom the Debtor owes money or property):

Name and address where notices should be sent:

28445961000031
HAYMARKET MEDIA, INC.
ATTN: ~~RUPERT HEGELTINE, CHAIRMAN~~
114 WEST 26TH STREET
3RD FLOOR
NEW YORK, NY 10001

[ ] Check this box to indicate that this claim amends a previously filed claim.

Court Claim Number:_____
(If known)

Filed on:_____

Name and address where payment should be sent (if different from above):

ATTN: MICHAEL KRIAK CFO

Telephone number: 646-638-6050

[ ] Check this box if you are aware that anyone else has filed a proof of claim relating to your claim. Attach copy of statement giving particulars.

[ ] Check this box if you are the Debtor or trustee in this case.

If an amount is identified above, you have a claim scheduled by one of the Debtors as shown. Please review the bar date notice to determine whether you must file a proof of claim to preserve your rights. The bar date notice is available online at www.bmcgroup.com/graceway or upon request at the address on the back of this form.

THIS SPACE IS FOR COURT USE ONLY

3. Amount of Claim as of Date Case Filed: $ 89,072.78 INVOICES ENCLOSED

If all or part of your claim is secured, complete item 6 below; however, if all of your claim is unsecured, do not complete item 6.
If all or part of your claim is entitled to priority, complete item 7.

[ ] Check this box if claim includes interest or other charges in addition to the principal amount of claim. Attach itemized statement of interest or charges.

4. Basis for Claim: NON PAYMENT FOR SERVICES RENDERED
(See instruction #4 on reverse side.)

5. Last four digits of any number by which creditor identifies Debtor: 0628
5a. Debtor may have scheduled account as: _____
(See instruction #5a on reverse side.)

6. Secured Claim (See instruction #6 on reverse side.)
Check the appropriate box if your claim is secured by a lien on property or a right of setoff and provide the requested information.

Nature of property or right of setoff: [ ] Real Estate [ ] Motor Vehicle [ ] Equipment [ ] Other

Describe:

Value of Property: $_____ **Annual Interest Rate** ____%

Amount of arrearage and other charges as of time case filed included in secured claim, if any: $_____ **Basis for perfection:** _____

Amount of Secured Claim: $_____ **Amount Unsecured: $**_____

RECEIVED
DEC 01 2011
BMC GROUP

7. Amount of Claim Entitled to Priority under 11 U.S.C. § 507(a). If any portion of your claim falls in one of the following categories, check the box and state the amount.

Specify the priority of the claim.

[ ] Domestic support obligations under 11 U.S.C. § 507(a)(1)(A) or (a)(1)(B).

[ ] Wages, salaries, or commissions (up to $11,725*) earned within 180 days before filing of the bankruptcy petition or cessation of the debtor's business, whichever is earlier – 11 U.S.C. § 507(a)(4).

[ ] Contributions to an employee benefit plan – 11 U.S.C. § 507(a)(5).

[ ] Up to $2,600* of deposits toward purchase, lease, or rental of property or services for personal, family, or household use – 11 U.S.C. § 507 (a)(7).

[ ] Taxes or penalties owed to governmental units – 11 U.S.C. § 507 (a)(8).

[ ] Other – Specify applicable paragraph of 11 U.S.C. § 507(a)(____).

Amount entitled to priority:

$_____

**Amounts are subject to adjustment on 4/1/13 and every 3 years thereafter with respect to cases commenced on or after the date of adjustment.*

8. Credits: The amount of all payments on this claim has been credited for the purpose of making this proof of claim.

9. Documents: Attach redacted copies of any documents that support the claim, such as promissory notes, purchase orders, invoices, itemized statements or running accounts, contracts, judgments, mortgages, and security agreements. You may also attach a summary. Attach redacted copies of documents providing evidence of perfection of a security interest. You may also attach a summary. *(See instruction 9 and definition of "redacted" on reverse side.)*

DO NOT SEND ORIGINAL DOCUMENTS. ATTACHED DOCUMENTS MAY BE DESTROYED AFTER SCANNING.

If the documents are not available, please explain in an attachment.

10. Signature: The person filing this claim must sign it. Sign and print name and title, if any, of the creditor or other person authorized to file this claim and state address and telephone number if different from the notice address above. Attach copy of power of attorney, if any.

FOR COURT USE ONLY
Graceway Pharmaceuticals LLC
00074

Date: 11/30/11 Signature: _____ Printed Name: LUIS M. PEREZ
CREDIT MANAGER

INSTRUCTIONS FOR PROOF OF CLAIM FORM

The instructions and definitions below are general explanations of the law. In certain circumstances, such as bankruptcy cases not filed voluntarily by the Debtor, there may be exceptions to these general rules. The attorneys for the Debtors and their court-appointed claims agent are not authorized and are not providing you with any legal advice.

PLEASE SEND YOUR ORIGINAL, COMPLETED CLAIM FORM AS FOLLOWS: **IF BY MAIL:** BMC GROUP, INC., ATTN: GRACEWAY PHARMACEUTICALS CLAIMS PROCESSING, P.O. BOX 3020, CHANHASSEN, MN 55317-3020. **IF BY HAND DELIVERY OR OVERNIGHT COURIER:** BMC GROUP, INC., ATTN: GRACEWAY PHARMACEUTICALS CLAIMS PROCESSING, 18750 LAKE DRIVE EAST CHANHASSEN, MN 55317. **ANY PROOF OF CLAIM SUBMITTED BY FACSIMILE OR E-MAIL WILL NOT BE ACCEPTED.**

THE GENERAL BAR DATE FOR CLAIMS IN THESE CHAPTER 11 CASES IS DECEMBER 30, 2011 4:00 P.M. (PREVAILING EASTERN TIME). THE GOVERNMENTAL BAR DATE FOR CLAIMS OF GOVERNMENTAL ENTITIES IN THESE CHAPTER 11 CASES IS MARCH 27, 2012 AT 4:00 P.M. (PREVAILING EASTERN TIME).

1. **Court, Name of Debtor, and Case Number:**
   These Chapter 11 cases were commenced in the United States Bankruptcy Court for the District of Delaware. You must select the Debtor against which you are asserting your claim. **A SEPARATE PROOF OF CLAIM FORM MUST BE FILED AGAINST EACH DEBTOR.**
2. **Creditor's Name and Address:**
   Fill in the name of the person or entity asserting a claim and the name and address of the person who should receive notices issued during the bankruptcy case. Please provide us with a valid email address. A separate space is provided for the payment address if it differs from the notice address. The creditor has a continuing obligation to keep the court informed of its current address. See Federal Rule of Bankruptcy Procedure (FRBP) 2002(g).
3. **Amount of Claim as of Date Case Filed:**
   State the total amount owed to the creditor on the date of the bankruptcy filing. Follow the instructions concerning whether to complete items 6 and 7. Check the box if interest or other charges are included in the claim.
4. **Basis for Claim:**
   State the type of debt or how it was incurred. Examples include goods sold, money loaned, services performed, personal injury/wrongful death, car loan, mortgage note, and credit card. If the claim is based on the delivery of health care goods or services, limit the disclosure of the goods or services so as to avoid embarrassment or the disclosure of confidential health care information. You may be required to provide additional disclosure if the trustee or another party in interest files an objection to your claim.
5. **Last Four Digits of Any Number by Which Creditor Identifies Debtor:**
   State only the last four digits of the Debtor's account or other number used by the creditor to identify the Debtor.
   5a. Debtor May Have Scheduled Account As:
   Use this space to report a change in the creditor's name, a transferred claim, or any other information that clarifies a difference between this proof of claim and the claim as scheduled by the Debtor.
6. **Secured Claim:**
   Check the appropriate box and provide the requested information if the claim is fully or partially secured. Skip this section if the claim is entirely unsecured. (See DEFINITIONS, below.) State the type and the value of property that secures the claim, attach copies of lien documentation, and state annual interest rate and the amount past due on the claim as of the date of the bankruptcy filing.
7. **Amount of Claim Entitled to Priority Under 11 U.S.C. § 507(a):**
   If any portion of your claim falls in one or more of the listed categories, check the appropriate box(es) and state the amount entitled to priority. (See DEFINITIONS, below.) A claim may be partly priority and partly non-priority. For example, in some of the categories, the law limits the amount entitled to priority.
8. **Credits:**
   An authorized signature on this proof of claim serves as an acknowledgment that when calculating the amount of the claim, the creditor gave the Debtor credit for any payments received toward the debt.
9. **Documents:**
   Attach to this proof of claim form redacted copies documenting the existence of the debt and of any lien securing the debt. You may also attach a summary. You must also attach copies of documents that evidence perfection of any security interest. You may also attach a summary. FRBP 3001(c) and (d). If the claim is based on the delivery of health care goods or services, see instruction 4. Do not send original documents, as attachments may be destroyed after scanning.
10. **Date and Signature:**
    The person filing this proof of claim must sign and date it. FRBP 9011. Print the name and title, if any, of the creditor or other person authorized to file this claim. State the filer's address and telephone number if it differs from the address given on the top of the form for purposes of receiving notices. Attach a complete copy of any power of attorney. Criminal penalties apply for making a false statement on a proof of claim.

DEFINITIONS

Debtor
A Debtor is the person, corporation, or other entity that has filed a bankruptcy case.
The Debtors in these Chapter 11 cases are:

Graceway Pharmaceuticals, LLC (11-13036)
Graceway Pharma Holding Corp. (11-13037)
Graceway Holdings, LLC (11-13038)
Chester Valley Holdings, LLC (11-13039)
Chester Valley Pharmaceuticals, LLC (11-13041)
Graceway Canada Holdings, Inc. (11-13042)
Graceway International, Inc. (11-13043)

Certain of the Debtors were known by other names within the past six years; such former names are identified in the notice of commencement.

Creditor
A creditor is the person, corporation, or other entity owed a debt by the Debtor on the date of the bankruptcy filing.

Claim
A claim is the creditor's right to receive payment on a debt owed by the Debtor that arose on the date of the bankruptcy filing. See 11 U.S.C. § 101(5). A claim may be secured or unsecured.

Proof of Claim
A proof of claim is a form used by the creditor to indicate the amount of the debt owed by the Debtor on the date of the bankruptcy filing. The creditor must file the form with The Garden City Group, Inc. as described in the instructions above.

Secured Claim Under 11 U.S.C. § 506(a)
A secured claim is one backed by a lien on property of the Debtor. The claim is secured so long as the creditor has the right to be paid from the property prior to other creditors. The amount of the secured claim can-not exceed the value of the property. Any amount owed to the creditor in excess of the value of the property is an unsecured claim. Examples of liens on property include a mortgage on real estate or a security interest in a car. A lien may be voluntarily granted by a Debtor or may be obtained through a court proceeding. In some states, a court judgment is a lien. A claim also may be secured if the creditor owes the Debtor money (has a right to setoff).

Section 503(b)(9) Claim
A Section 503(b)(9) claim is a claim for the value of any goods received by the Debtor within 20 days before the date of commencement of a bankruptcy case in which the goods have been sold to the Debtor in the ordinary course of such Debtor's business.

Unsecured Claim
An unsecured claim is one that does not meet the requirements of a secured claim. A claim may be partly unsecured if the amount of the claim exceeds the value of the property on which the creditor has a lien.

Claim Entitled to Priority Under 11 U.S.C. § 507(a)
Priority claims are certain categories of unsecured claims that are paid from the available money or property in a bankruptcy case before other unsecured claims.

Redacted
A document has been redacted when the person filing it has masked, edited out, or otherwise deleted, certain information. A creditor should redact and use only the last four digits of any social-security, individual's tax-identification, or financial-account number, all but the initials of a minor's name and only the year of any person's date of birth.

Evidence of Perfection
Evidence of perfection may include a mortgage, lien, certificate of title, financing statement, or other document showing that the lien has been filed or recorded.

INFORMATION

Acknowledgment of Filing of Claim
To receive acknowledgment of your filing, please provide a stamped self-addressed envelope and a copy of this proof of claim when you file the original claim.

Offers to Purchase a Claim
Certain entities are in the business of purchasing claims for an amount less than the face value of the claims. One or more of these entities may contact the creditor and offer to purchase the claim. Some of the written communications from these entities may easily be confused with official court documentation or communications from the Debtor. These entities do not represent the bankruptcy court or the Debtor. The creditor has no obligation to sell its claim. However, if the creditor decides to sell its claim, any transfer of such claim is subject to FRBP 3001(e), any applicable provisions of the Bankruptcy Code (11 U.S.C. § 101 et seq.), and any applicable orders of the bankruptcy court.

S60628

SH Media, LLC
11 Rose Meadow Way
Aquinnah, MA 02535
508-645-9022

INSERTION ORDER

To:	Alison McCauley	Date: 7/28/11	
Fax No.:	646-638-6117	Insertion Order No.: GRW11108	
Tel No.:	646-638-6098		
From:	Stefanie Hecht 508-645-9022, 508-645-9021 Fax		
For Insertion In:	CLINICAL ADVISOR		

CLIENT:		Graceway Pharmaceuticals
PRODUCT:		ZYCLARA
DATE OF ISSUE:		September
AD UNIT:		Page 4CB + Page BW
AD NO.:		ZYC1110186
HEADLINE:		"Effectively Clears Genital Warts"
POSITION:		Far forward
TIME RATE -	SPACE:	12x Continuity Rate
	COLOR:	1x
NET COST:		$8,653.00
MATERIAL FROM:		Repeat from July
SPECIAL INSTRUCTIONS:		

provisional:
Calculation:
Gross: 10,180
Net: 8,653

NAME DATE

Please send invoices to: Graceway Pharmaceuticals, Attn: Accounts Payable, 340 Martin Luther King Jr Blvd, Suite 400, Bristol, TN 37620

IF INCLUDED, PRESCRIBING INFORMATION MUST RUN IMMEDIATELY ADJACENT TO AD

PLEASE SEND TWO (2) TEAR SHEETS ALONG WITH INVOICE

HAYMARKET MEDIA INC.

114 West 26th Street - 3rd Floor
New York, NY 10001
Tel (646) 638-6000

COPY INVOICE

ACCOUNTS PAYABLES
GRACEWAY PHARMACEUTICALS
340 MARTIN LUTHER KING BLVD.
SUITE 400, BRISTOL, TN
37620

Invoice No:	46669
Date:	09/26/11
Your Order Ref :	GRW11108
Account No :	560628

Description		Value
Your Client:	**Graceway Pharmaceuticals**	
Publication:	**Clinical Advisor**	
		8,653.00
Cover Date :	01-September-2011	
Your Contact:	Accounts Payables	
Our Salesperson:	Alison McCauley	
Our Booking Ref:	0000100758	
Product:	Zyclara	
Frequency Rate:	12	
Page Number/s:	73,74	
PO#		
		8,653.00
	Net Value	8,653.00

REMITTANCE RECORD

Customer :	GRACEWAY PHARMACEUTICALS	**Payment Terms**	Net 30 Days
Account No :	560628	**Due Date**	**10/26/11**
Invoice No :	46669	**Total Due** USD	8,653.00

Amount Enclosed $

Cheque Number

Please make all cheques payable to **Haymarket Media, Inc. PO BOX 512368, Philadelphia, PA 19175-2368** and remit to this address with this bottom portion of the invoice. Thank You.

What patients want in the treatment of external genital warts (EGW)...

Effectively clears genital warts and keeps patients clear

Short treatment, daily dosing

- Applied once daily for up to 8 weeks

Significant clearance in females

- 37% complete clearance, 48% partial clearance[1]
  - Partial clearance defined as ≥75% reduction in EGW count from baseline

Patients who clear with Zyclara can expect to remain clear

- Only 15% of patients had a recurrence at 12 weeks posttreatment[1]

Tough on warts, easy on patients

- Low incidence of treatment-related adverse events at the application site: itching (3%), irritation (6%), or pain (7%)[1]
- Local skin reactions, most of which were mild to moderate, included severe erythema (9%) and severe erosion/ulceration (11%)[1]

Zyclara®
(imiquimod) Cream
3.75%

Zyclara Cream is indicated for the treatment of external genital and perianal warts/condyloma acuminata in patients 12 years or older.

In clinical studies, the most frequently reported adverse reactions were local skin and application site reactions. These reactions included erythema, edema, erosion or ulceration, and exudate at the genital wart site. Most local skin reactions were rated as mild to moderate. Intense local inflammatory reactions and/or flu-like systemic signs and symptoms can occur. Dosing interruptions may be required.

Avoid concomitant use of Zyclara Cream and any other imiquimod cream because of increased risk for adverse reactions.

Zyclara Cream is not recommended for the treatment of urethral, intra-vaginal, cervical, rectal, or intra-anal human papilloma viral disease as it has not been studied.

The effect of Zyclara Cream on the transmission of genital warts is unknown. Zyclara Cream may weaken condoms and diaphragms. Sexual contact should be avoided while the cream is on the skin.

Please see Brief Summary of Prescribing Information on adjacent page.

Reference: 1. Data on file. Graceway Pharmaceuticals, LLC.

Zyclara® [zi-clar-a]
(imiquimod) Cream 3.75%

BRIEF SUMMARY OF PRESCRIBING INFORMATION

SEE PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

INDICATIONS AND USAGE

External Genital Warts

ZYCLARA Cream is indicated for the treatment of external genital and perianal warts (EGW)/condyloma acuminata in patients 12 years or older.

Limitations of Use

Treatment with ZYCLARA has not been studied for prevention or transmission of HPV.

Unevaluated Populations

The safety and efficacy of ZYCLARA Cream have not been established in the treatment of:
- urethral, intra-vaginal, cervical, rectal or intra-anal human papilloma viral disease.
- actinic keratosis when treated with more than one 2-cycle treatment course in the same area.
- patients with xeroderma pigmentosum.
- superficial basal cell carcinoma.
- immunosuppressed patients.

CONTRAINDICATIONS None.

WARNINGS AND PRECAUTIONS

Local Skin Reactions

Intense local skin reactions including skin weeping or erosion can occur after a few applications of ZYCLARA Cream and may require an interruption of dosing. ZYCLARA Cream has the potential to exacerbate inflammatory conditions of the skin, including chronic graft versus host disease.

Administration of ZYCLARA Cream is not recommended until the skin is healed from any previous drug or surgical treatment.

Systemic Reactions

Flu-like signs and symptoms may accompany, or even precede, local skin reactions and may include fatigue, nausea, fever, myalgias, arthralgias, malaise and chills. An interruption of dosing and assessment of the patient should be considered.

Lymphadenopathy occurred in 2% of subjects with actinic keratosis treated with ZYCLARA Cream. This reaction resolved in all subjects by 4 weeks after completion of treatment.

Ultraviolet Light Exposure Risks

Exposure to sunlight (including sunlamps) should be avoided or minimized during use of ZYCLARA Cream. Patients should be warned to use protective clothing (e.g., a hat) when using ZYCLARA Cream. Patients with sunburn should be advised not to use ZYCLARA Cream until fully recovered. Patients who may have considerable sun exposure, e.g. due to their occupation, and those patients with inherent sensitivity to sunlight should exercise caution when using ZYCLARA Cream.

In an animal photo-carcinogenicity study, imiquimod cream shortened the time to skin tumor formation. The enhancement of ultraviolet carcinogenicity is not necessarily dependent on phototoxic mechanisms. Therefore, patients should minimize or avoid natural or artificial sunlight exposure.

Increased Risk of Adverse Reactions with Concomitant Imiquimod Use

Concomitant use of ZYCLARA and any other imiquimod products, in the same treatment area, should be avoided since they contain the same active ingredient (imiquimod) and may increase the risk for and severity of local skin reactions.

The safety of concomitant use of ZYCLARA Cream and any other imiquimod products has not been established and should be avoided since they contain the same active ingredient (imiquimod) and may increase the risk for and severity of systemic reactions.

Immune Cell Activation in Autoimmune Disease

ZYCLARA Cream should be used with caution in patients with pre-existing autoimmune conditions because imiquimod activates immune cells.

ADVERSE REACTIONS

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Clinical Trials Experience: External Genital Warts

In two double-blind, placebo-controlled studies 602 subjects applied up to one packet of ZYCLARA Cream or vehicle daily for up to 8 weeks.

The most frequently reported adverse reactions were application site reactions and local skin reactions. Selected adverse reactions are listed in Table 1.

Table 1: Selected Adverse Reactions Occurring in ≥2% of ZYCLARA Treated Subjects and at a Greater Frequency than with Vehicle in the Combined Trials (EGW)

Preferred Term	ZYCLARA Cream 3.75% (N=400)	Vehicle Cream (N=202)
Application site pain	28 (7%)	1 (<1%)
Application site irritation	24 (6%)	2 (1%)
Application site pruritus	11 (3%)	2 (1%)
Vaginitis bacterial*	6 (3%)	2 (2%)
Headache	6 (2%)	1 (<1%)

*Percentage based on female population of 6/216 for ZYCLARA Cream 3.75% and 2/106 for vehicle cream

Local skin reactions were recorded as adverse reactions only if they extended beyond the treatment area, if they required any medical intervention, or they resulted in patient discontinuation from the study. The incidence and severity of selected local skin reactions are shown in Table 2.

Table 2: Selected Local Skin Reactions in the Treatment Area Assessed by the Investigator (EGW)

All grades*, (%)	Severe, (%)	ZYCLARA Cream 3.75% (N=400)	Vehicle Cream (N=202)
Erythema*		70%	27%
	Severe erythema	9%	<1%
Edema*		41%	8%
	Severe edema	2%	0%
Erosion/ulceration*		36%	4%
	Severe erosion/ulceration	11%	<1%
Exudate*		34%	2%
	Severe exudate	2%	0%

*Mild, Moderate, or Severe

The frequency and severity of local skin reactions were similar in both genders, with the following exceptions: a) flaking/scaling occurred in 40% of men and in 26% of women and b) scabbing/crusting occurred in 34% of men and in 18% of women.

In the clinical trials, 32% (126/400) of subjects who used ZYCLARA Cream and 2% (4/202) of subjects who used vehicle cream discontinued treatment temporarily (required rest periods) due to adverse local skin reactions, and 1% (3/400) of subjects who used ZYCLARA Cream discontinued treatment permanently due to local skin/application site reactions.

Other adverse reactions reported in subjects treated with ZYCLARA Cream include: rash, back pain, application site rash, application site cellulitis, application site excoriation, application site bleeding, scrotal pain, scrotal erythema, scrotal ulcer, scrotal edema, sinusitis, nausea, pyrexia, and influenza-like symptoms.

Postmarketing Experience

The following adverse reactions have been identified during post-approval use of imiquimod. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Application Site Disorders: tingling at the application site.

Body as a Whole: angioedema.

Cardiovascular: capillary leak syndrome, cardiac failure, cardiomyopathy, pulmonary edema, arrhythmias (tachycardia, supraventricular tachycardia, atrial fibrillation, palpitations), chest pain, ischemia, myocardial infarction, syncope.

Endocrine: thyroiditis.

Gastro-Intestinal System Disorders: abdominal pain.

Hematological: decreases in red cell, white cell and platelet counts (including idiopathic thrombocytopenic purpura), lymphoma.

Hepatic: abnormal liver function.

Infections and Infestations: herpes simplex.

Musculo-Skeletal System Disorders: arthralgia.

Neuropsychiatric: agitation, cerebrovascular accident, convulsions (including febrile convulsions), depression, insomnia, multiple sclerosis aggravation, paresis, suicide.

Respiratory: dyspnea.

Urinary System Disorders: proteinuria, urinary retention, dysuria.

Skin and Appendages: exfoliative dermatitis, erythema multiforme, hyperpigmentation, hypertrophic scar, hypopigmentation.

Vascular: Henoch-Schonlein purpura syndrome.

USE IN SPECIFIC POPULATIONS

Pregnancy Pregnancy Category C:

There are no adequate and well-controlled studies in pregnant women. ZYCLARA Cream should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

The animal multiples of human exposure calculations were based on daily dose comparisons for the reproductive toxicology studies described in this label. The animal multiples of human exposure were based on weekly dose comparisons for the carcinogenicity studies described in this label. For the animal multiple of human exposure ratios presented in this label, the Maximum Recommended Human Dose (MRHD) was set at 2 packets (500 mg cream) per treatment of actinic keratosis with ZYCLARA Cream (imiquimod 3.75%, 18.75 mg imiquimod) for BSA comparison. The maximum human AUC value obtained in the treatment of external genital and perianal warts was higher than that obtained in the treatment of actinic keratosis and was used in the calculation of animal multiples of MRHD that were based on AUC comparison.

Systemic embryofetal development studies were conducted in rats and rabbits. Oral doses of 1, 5 and 20 mg/kg/day imiquimod were administered during the period of organogenesis (gestational days 6 – 15) to pregnant female rats. In the presence of maternal toxicity, fetal effects noted at 20 mg/kg/day (163X MRHD based on AUC comparisons) included increased resorptions, decreased fetal body weights, delays in skeletal ossification, bent limb bones, and two fetuses in one litter (2 of 1567 fetuses) demonstrated exencephaly, protruding tongues and low-set ears. No treatment related effects on embryofetal toxicity or teratogenicity were noted at 5 mg/kg/day (28X MRHD based on AUC comparisons).

Intravenous doses of 0.5, 1 and 2 mg/kg/day imiquimod were administered during the period of organogenesis (gestational days 6 – 18) to pregnant female rabbits. No treatment related effects on embryofetal toxicity or teratogenicity were noted at 2 mg/kg/day (2.1X MRHD based on BSA comparisons), the highest dose evaluated in this study, or 1 mg/kg/day (115X MRHD based on AUC comparisons).

A combined fertility and peri- and post-natal development study was conducted in rats. Oral doses of 1, 1.5, 3 and 6 mg/kg/day imiquimod were administered to male rats from 70 days prior to mating through the mating period and to female rats from 14 days prior to mating through parturition and lactation. No effects on growth, fertility, reproduction or post-natal development were noted at doses up to 6 mg/kg/day (25X MRHD based on AUC comparisons), the highest dose evaluated in this study. In the absence of maternal toxicity, bent limb bones were noted in the F1 fetuses at a dose of 6 mg/kg/day (25X MRHD based on AUC comparisons). This fetal effect was also noted in the oral rat embryofetal development study conducted with imiquimod. No treatment related effects on teratogenicity were noted at 3 mg/kg/day (12X MRHD based on AUC comparisons).

Nursing Mothers

It is not known whether imiquimod is excreted in human milk following use of ZYCLARA Cream. Because many drugs are excreted in human milk, caution should be exercised when ZYCLARA Cream is administered to nursing women.

Pediatric Use

Safety and efficacy in patients with external genital/perianal warts below the age of 12 years have not been established.

Geriatric Use

Clinical studies of ZYCLARA Cream for EGW did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Of the 400 subjects treated with ZYCLARA Cream in the EGW clinical studies, 5 subjects (1%) were 65 years or older.

OVERDOSAGE

Topical overdosing of ZYCLARA Cream could result in an increased incidence of severe local skin reactions and may increase the risk for systemic reactions.

Hypotension was reported in a clinical trial following multiple oral imiquimod doses of >200 mg (equivalent to ingestion of the imiquimod content of more than 21 packets of ZYCLARA). The hypotension resolved following oral or intravenous fluid administration.

Rx Only

GRACEWAY® PHARMACEUTICALS

Manufactured by
3M Health Care Limited
Loughborough LE11 1EP England
Distributed by
Graceway Pharmaceuticals, LLC
Bristol, TN 37620

Issued: March 2011
ZYC031137

S60628 ✓

SH Media, LLC
11 Rose Meadow Way
Aquinnah, MA 02535
508-645-9022

CMS

INSERTION ORDER

To: Dominic Barone

Date: 7/28/11

Fax No.: 646-638-6120

Insertion Order No.: GRW11114

Tel No.: 646-638-6097

From: Stefanie Hecht 508-645-9022, 508-645-9021 Fax

For Insertion In: JAAPA

PO# 4500010169

CLIENT:	Graceway Pharmaceuticals
PRODUCT:	ZYCLARA
DATE OF ISSUE:	September
AD UNIT:	Page 4CB + Page BW
AD NO.:	ZYC1110188
HEADLINE:	"Thwarted"
POSITION:	Far forward
TIME RATE - SPACE:	48x
COLOR:	1x
NET COST:	$8,321.50
MATERIAL FROM:	Repeat from July
SPECIAL INSTRUCTIONS:	

Gross: 9,790

Net: 8,321.50

NAME DATE

Please send Invoices to: Graceway Pharmaceuticals, Attn: Accounts Payable, 340 Martin Luther King Jr Blvd, Suite 400, Bristol, TN 37620

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HAYMARKET MEDIA INC.

114 West 26th Street - 3rd Floor
New York, NY 10001
Tel (646) 638-6000

COPY INVOICE

ACCOUNTS PAYABLES
GRACEWAY PHARMACEUTICALS
340 MARTIN LUTHER KING BLVD.
SUITE 400, BRISTOL, TN
37620

Invoice No:	46605
Date:	09/26/11
Your Order Ref :	GRW11114
Account No :	560628

Description		Value
Your Client:	**Graceway Pharmaceuticals**	
Publication:	**JAAPA**	
		8,321.50
Cover Date :	01-September-2011	
Your Contact:	Accounts Payables	
Our Salesperson:	Dominic Barone	
Our Booking Ref:	0000100695	
Product:	Zyclara	
Frequency Rate:	48	
Page Number/s:	13,14	
		8,321.50
	Net Value	8,321.50

REMITTANCE RECORD

Customer :	GRACEWAY PHARMACEUTICALS	**Payment Terms**	Net 30 Days
Account No :	560628	**Due Date**	**10/26/11**
Invoice No :	46605	**Total Due** USD	8,321.50

Amount Enclosed $

Cheque Number

Please make all cheques payable to **Haymarket Media, Inc. PO BOX 512368, Philadelphia, PA 19175-2368** and remit to this address with this bottom portion of the invoice. Thank You.

GENITAL WARTS

THWARTED!

Short treatment, daily dosing

- Applied once daily for up to 8 weeks[1]

Significant clearance of external genital warts[1]

In females–

- 37% complete clearance; 48% partial clearance

In males–

- 19% complete clearance; 27% partial clearance
  – Partial clearance defined as ≥75% reduction in EGW count from baseline

Many patients who cleared with Zyclara remained clear[1]

- Only 15% of patients had a recurrence at 12 weeks posttreatment

Tough on warts, easy on patients

- Low incidence of treatment-related adverse events at the application site: itching (3%), irritation (6%), or pain (7%)[1]
- Local skin reactions, most of which were mild to moderate, included severe erythema (9%) and severe erosion/ulceration (11%)[1]

Zyclara®
(imiquimod) Cream
3.75%

Zyclara Cream is indicated for the treatment of external genital and perianal warts/condyloma acuminata in patients 12 years or older.

In clinical studies, the most frequently reported adverse reactions were local skin and application site reactions. These reactions included erythema, edema, erosion or ulceration, and exudate at the genital wart site. Most local skin reactions were rated as mild to moderate. Intense local inflammatory reactions and/or flu-like systemic signs and symptoms can occur. Dosing interruptions may be required.

Avoid concomitant use of Zyclara Cream and any other imiquimod cream because of increased risk for adverse reactions.

Zyclara Cream is not recommended for the treatment of urethral, intra-vaginal, cervical, rectal, or intra-anal human papilloma viral disease as it has not been studied.

The effect of Zyclara Cream on the transmission of genital warts is unknown. Zyclara Cream may weaken condoms and diaphragms. Sexual contact should be avoided while the cream is on the skin.

Please see Brief Summary of Prescribing Information on adjacent page.

Reference: 1. Data on file, Graceway Pharmaceuticals, LLC.

GRACEWAY® PHARMACEUTICALS

Zyclara® [zi-clar-a]
(imiquimod) Cream 3.75%

BRIEF SUMMARY OF PRESCRIBING INFORMATION

SEE PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

INDICATIONS AND USAGE

External Genital Warts

ZYCLARA Cream is indicated for the treatment of external genital and perianal warts (EGW)/condyloma acuminata in patients 12 years or older.

Limitations of Use

Treatment with ZYCLARA has not been studied for prevention or transmission of HPV.

Unevaluated Populations

The safety and efficacy of ZYCLARA Cream have not been established in the treatment of:
- urethral, intra-vaginal, cervical, rectal or intra-anal human papilloma viral disease.
- actinic keratosis when treated with more than one 2-cycle treatment course in the same area.
- patients with xeroderma pigmentosum.
- superficial basal cell carcinoma.
- immunosuppressed patients.

CONTRAINDICATIONS None.

WARNINGS AND PRECAUTIONS

Local Skin Reactions

Intense local skin reactions including skin weeping or erosion can occur after a few applications of ZYCLARA Cream and may require an interruption of dosing. ZYCLARA Cream has the potential to exacerbate inflammatory conditions of the skin, including chronic graft versus host disease.

Administration of ZYCLARA Cream is not recommended until the skin is healed from any previous drug or surgical treatment.

Systemic Reactions

Flu-like signs and symptoms may accompany, or even precede, local skin reactions and may include fatigue, nausea, fever, myalgias, arthralgias, malaise and chills. An interruption of dosing and assessment of the patient should be considered.

Lymphadenopathy occurred in 2% of subjects with actinic keratosis treated with ZYCLARA Cream. This reaction resolved in all subjects by 4 weeks after completion of treatment.

Ultraviolet Light Exposure Risks

Exposure to sunlight (including sunlamps) should be avoided or minimized during use of ZYCLARA Cream. Patients should be warned to use protective clothing (e.g., a hat) when using ZYCLARA Cream. Patients with sunburn should be advised not to use ZYCLARA Cream until fully recovered. Patients who may have considerable sun exposure, e.g. due to their occupation, and those patients with inherent sensitivity to sunlight should exercise caution when using ZYCLARA Cream.

In an animal photo-carcinogenicity study, imiquimod cream shortened the time to skin tumor formation. The enhancement of ultraviolet carcinogenicity is not necessarily dependent on phototoxic mechanisms. Therefore, patients should minimize or avoid natural or artificial sunlight exposure.

Increased Risk of Adverse Reactions with Concomitant Imiquimod Use

Concomitant use of ZYCLARA and any other imiquimod products, in the same treatment area, should be avoided since they contain the same active ingredient (imiquimod) and may increase the risk for and severity of local skin reactions.

The safety of concomitant use of ZYCLARA Cream and any other imiquimod products has not been established and should be avoided since they contain the same active ingredient (imiquimod) and may increase the risk for and severity of systemic reactions.

Immune Cell Activation in Autoimmune Disease

ZYCLARA Cream should be used with caution in patients with pre-existing autoimmune conditions because imiquimod activates immune cells.

ADVERSE REACTIONS

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Clinical Trials Experience: External Genital Warts

In two double-blind, placebo-controlled studies 602 subjects applied up to one packet of ZYCLARA Cream or vehicle daily for up to 8 weeks.

The most frequently reported adverse reactions were application site reactions and local skin reactions. Selected adverse reactions are listed in Table 1.

Table 1: Selected Adverse Reactions Occurring in ≥2% of ZYCLARA Treated Subjects and at a Greater Frequency than with Vehicle in the Combined Trials (EGW)

Preferred Term	ZYCLARA Cream 3.75% (N=400)	Vehicle Cream (N=202)
Application site pain	28 (7%)	1 (<1%)
Application site irritation	24 (6%)	2 (1%)
Application site pruritus	11 (3%)	2 (1%)
Vaginitis bacterial*	6 (3%)	2 (2%)
Headache	6 (2%)	1 (<1%)

*Percentage based on female population of 6/216 for ZYCLARA Cream 3.75% and 2/106 for vehicle cream

Local skin reactions were recorded as adverse reactions only if they extended beyond the treatment area, if they required any medical intervention, or they resulted in patient discontinuation from the study. The incidence and severity of selected local skin reactions are shown in Table 2.

Table 2: Selected Local Skin Reactions in the Treatment Area Assessed by the Investigator (EGW)

All grades*, (%)	Severe, (%)	ZYCLARA Cream 3.75% (N=400)	Vehicle Cream (N=202)
Erythema*		70%	27%
	Severe erythema	9%	<1%
Edema*		41%	8%
	Severe edema	2%	0%
Erosion/ulceration*		36%	4%
	Severe erosion/ulceration	11%	<1%
Exudate*		34%	2%
	Severe exudate	2%	0%

*Mild, Moderate, or Severe

The frequency and severity of local skin reactions were similar in both genders, with the following exceptions: a) flaking/scaling occurred in 40% of men and in 26% of women and b) scabbing/crusting occurred in 34% of men and in 18% of women.

In the clinical trials, 32% (126/400) of subjects who used ZYCLARA Cream and 2% (4/202) of subjects who used vehicle cream discontinued treatment temporarily (required rest periods) due to adverse local skin reactions, and 1% (3/400) of subjects who used ZYCLARA Cream discontinued treatment permanently due to local skin/application site reactions.

Other adverse reactions reported in subjects treated with ZYCLARA Cream include: rash, back pain, application site rash, application site cellulitis, application site excoriation, application site bleeding, scrotal pain, scrotal erythema, scrotal ulcer, scrotal edema, sinusitis, nausea, pyrexia, and influenza-like symptoms.

Postmarketing Experience

The following adverse reactions have been identified during post-approval use of imiquimod. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Application Site Disorders: tingling at the application site.

Body as a Whole: angioedema.

Cardiovascular: capillary leak syndrome, cardiac failure, cardiomyopathy, pulmonary edema, arrhythmias (tachycardia, supraventricular tachycardia, atrial fibrillation, palpitations), chest pain, ischemia, myocardial infarction, syncope.

Endocrine: thyroiditis.

Gastro-Intestinal System Disorders: abdominal pain.

Hematological: decreases in red cell, white cell and platelet counts (including idiopathic thrombocytopenic purpura), lymphoma.

Hepatic: abnormal liver function.

Infections and Infestations: herpes simplex.

Musculo-Skeletal System Disorders: arthralgia.

Neuropsychiatric: agitation, cerebrovascular accident, convulsions (including febrile convulsions), depression, insomnia, multiple sclerosis aggravation, paresis, suicide.

Respiratory: dyspnea.

Urinary System Disorders: proteinuria, urinary retention, dysuria.

Skin and Appendages: exfoliative dermatitis, erythema multiforme, hyperpigmentation, hypertrophic scar, hypopigmentation.

Vascular: Henoch-Schonlein purpura syndrome.

USE IN SPECIFIC POPULATIONS

Pregnancy Pregnancy Category C:

There are no adequate and well-controlled studies in pregnant women. ZYCLARA Cream should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

The animal multiples of human exposure calculations were based on daily dose comparisons for the reproductive toxicology studies described in this label. The animal multiples of human exposure were based on weekly dose comparisons for the carcinogenicity studies described in this label. For the animal multiple of human exposure ratios presented in this label, the Maximum Recommended Human Dose (MRHD) was set at 2 packets (500 mg cream) per treatment of actinic keratosis with ZYCLARA Cream (imiquimod 3.75%, 18.75 mg imiquimod) for BSA comparison. The maximum human AUC value obtained in the treatment of external genital and perianal warts was higher than that obtained in the treatment of actinic keratosis and was used in the calculation of animal multiples of MRHD that were based on AUC comparison.

Systemic embryofetal development studies were conducted in rats and rabbits. Oral doses of 1, 5 and 20 mg/kg/day imiquimod were administered during the period of organogenesis (gestational days 6 – 15) to pregnant female rats. In the presence of maternal toxicity, fetal effects noted at 20 mg/kg/day (163X MRHD based on AUC comparisons) included increased resorptions, decreased fetal body weights, delays in skeletal ossification, bent limb bones, and two fetuses in one litter (2 of 1567 fetuses) demonstrated exencephaly, protruding tongues and low-set ears. No treatment related effects on embryofetal toxicity or teratogenicity were noted at 5 mg/kg/day (28X MRHD based on AUC comparisons).

Intravenous doses of 0.5, 1 and 2 mg/kg/day imiquimod were administered during the period of organogenesis (gestational days 6 – 18) to pregnant female rabbits. No treatment related effects on embryofetal toxicity or teratogenicity were noted at 2 mg/kg/day (2.1X MRHD based on BSA comparisons), the highest dose evaluated in this study, or 1 mg/kg/day (11X MRHD based on AUC comparisons).

A combined fertility and peri- and post-natal development study was conducted in rats. Oral doses of 1, 1.5, 3 and 6 mg/kg/day imiquimod were administered to male rats from 70 days prior to mating through the mating period and to female rats from 14 days prior to mating through parturition and lactation. No effects on growth, fertility, reproduction or post-natal development were noted at doses up to 6 mg/kg/day (25X MRHD based on AUC comparisons), the highest dose evaluated in this study. In the absence of maternal toxicity, bent limb bones were noted in the F1 fetuses at a dose of 6 mg/kg/day (25X MRHD based on AUC comparisons). This fetal effect was also noted in the oral rat embryofetal development study conducted with imiquimod. No treatment related effects on teratogenicity were noted at 3 mg/kg/day (12X MRHD based on AUC comparisons).

Nursing Mothers

It is not known whether imiquimod is excreted in human milk following use of ZYCLARA Cream. Because many drugs are excreted in human milk, caution should be exercised when ZYCLARA Cream is administered to nursing women.

Pediatric Use

Safety and efficacy in patients with external genital/perianal warts below the age of 12 years have not been established.

Geriatric Use

Clinical studies of ZYCLARA Cream for EGW did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Of the 400 subjects treated with ZYCLARA Cream in the EGW clinical studies, 5 subjects (1%) were 65 years or older.

OVERDOSAGE

Topical overdosing of ZYCLARA Cream could result in an increased incidence of severe local skin reactions and may increase the risk for systemic reactions.

Hypotension was reported in a clinical trial following multiple oral imiquimod doses of >200 mg (equivalent to ingestion of the imiquimod content of more than 21 packets of ZYCLARA). The hypotension resolved following oral or intravenous fluid administration.

Rx Only

GRACEWAY® PHARMACEUTICALS

Manufactured by
3M Health Care Limited
Loughborough LE11 1EP England

Distributed by
Graceway Pharmaceuticals, LLC
Bristol, TN 37620

Issued: March 2011
ZYC031137

SH Media, LLC
11 Rose Meadow Way
Aquinnah, MA 02535
508-645-9022

INSERTION ORDER

To: Alison McCauley

Date: 9/8/11

Fax No.: 646-638-6117

Insertion Order No.: GRW11108

Tel No.: 646-638-6098

From: Stefanie Hecht 508-645-9022, 508-645-9021 Fax

For Insertion In: CLINICAL ADVISOR

CLIENT:	Graceway Pharmaceuticals
PRODUCT:	ZYCLARA
DATE OF ISSUE:	October
AD UNIT:	Page 4CB + Page BW
AD NO.:	ZYC1110186
HEADLINE:	"Effectively Clears Genital Warts"
POSITION:	Far forward
TIME RATE - SPACE:	12x Continuity Rate
COLOR:	1x
NET COST:	$8,653.00
MATERIAL FROM:	Repeat from September
SPECIAL INSTRUCTIONS:	

NAME DATE

Please send invoices to: Graceway Pharmaceuticals, Attn: Accounts Payable, 340 Martin Luther King Jr Blvd, Suite 400, Bristol, TN 37620

IF INCLUDED, PRESCRIBING INFORMATION MUST RUN IMMEDIATELY ADJACENT TO AD

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INVOICE

ACCOUNTS PAYABLES
GRACEWAY PHARMACEUTICALS
340 MARTIN LUTHER KING BLVD.
SUITE 400, BRISTOL, TN
37620

Invoice No:	CA102011
Date:	09/08/11
Your Order Ref :	GRW11108
Account No :	560628

Description		Value
Your Client:	**Graceway Pharmaceuticals**	
Publication:	**Clinical Advisor**	
		8,653.00
Cover Date :	01-October-2011	
Your Contact:	Accounts Payables	
Our Salesperson:	Alison McCauley	
Our Booking Ref:	0000100758	
Product:	Zyclara	
Frequency Rate:	12	
Page Number/s:	109, 110	
PO#4500010169		
		8,653.00
	Net Value	8,653.00

REMITTANCE RECORD

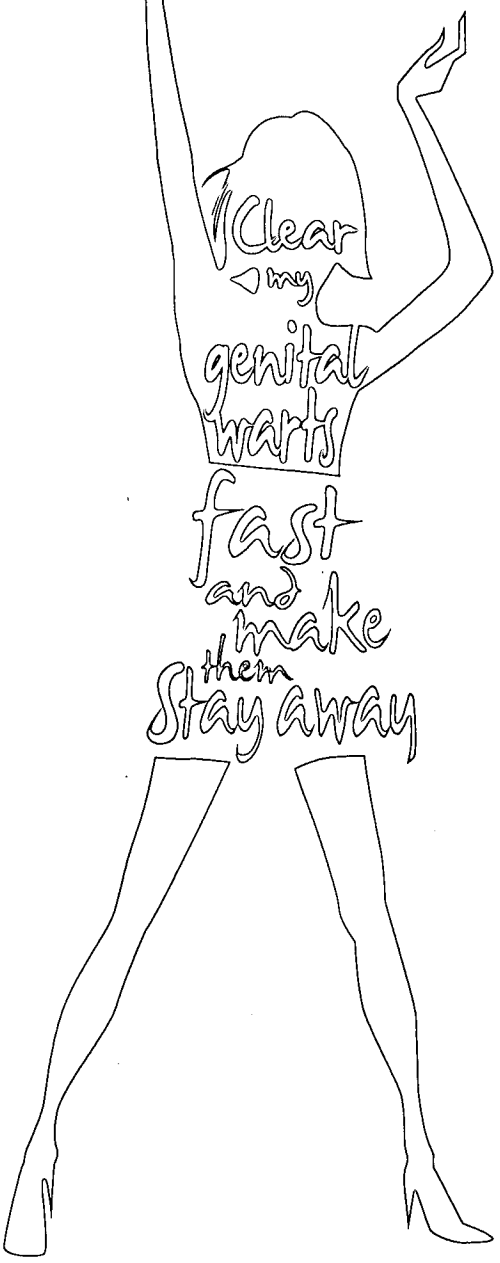
Customer :	GRACEWAY PHARMACEUTICALS	**Payment Terms**	Net 30 Days
Account No :	560628	**Due Date**	**10/07/11**
Invoice No :	46669	**Total Due** USD	8,653.00

Amount Enclosed $

Cheque Number

Please make all cheques payable to **Haymarket Media, Inc. PO BOX 512368, Philadelphia, PA 19175-2368** and remit to this address with this bottom portion of the invoice. Thank You.

What patients want in the treatment of external genital warts (EGW)...



Effectively clears genital warts and keeps patients clear

Short treatment, daily dosing

- Applied once daily for up to 8 weeks

Significant clearance in females

- 37% complete clearance, 48% partial clearance[1]
  - Partial clearance defined as ≥75% reduction in EGW count from baseline

Patients who clear with Zyclara can expect to remain clear

- Only 15% of patients had a recurrence at 12 weeks posttreatment[1]

Tough on warts, easy on patients

- Low incidence of treatment-related adverse events at the application site: itching (3%), irritation (6%), or pain (7%)[1]
- Local skin reactions, most of which were mild to moderate, included severe erythema (9%) and severe erosion/ulceration (11%)[1]

Zyclara®
(imiquimod) Cream
3.75%

Zyclara Cream is indicated for the treatment of external genital and perianal warts/condyloma acuminata in patients 12 years or older.

In clinical studies, the most frequently reported adverse reactions were local skin and application site reactions. These reactions included erythema, edema, erosion or ulceration, and exudate at the genital wart site. Most local skin reactions were rated as mild to moderate. Intense local inflammatory reactions and/or flu-like systemic signs and symptoms can occur. Dosing interruptions may be required.

Avoid concomitant use of Zyclara Cream and any other imiquimod cream because of increased risk for adverse reactions.

Zyclara Cream is not recommended for the treatment of urethral, intra-vaginal, cervical, rectal, or intra-anal human papilloma viral disease as it has not been studied.

The effect of Zyclara Cream on the transmission of genital warts is unknown. Zyclara Cream may weaken condoms and diaphragms. Sexual contact should be avoided while the cream is on the skin.

Please see Brief Summary of Prescribing Information on adjacent page.

Reference: 1. Data on file. Graceway Pharmaceuticals, LLC.

Zyclara® [zi-clar-a]
(imiquimod) Cream 3.75%

BRIEF SUMMARY OF PRESCRIBING INFORMATION

SEE PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

INDICATIONS AND USAGE

External Genital Warts

ZYCLARA Cream is indicated for the treatment of external genital and perianal warts (EGW)/condyloma acuminata in patients 12 years or older.

Limitations of Use

Treatment with ZYCLARA has not been studied for prevention or transmission of HPV.

Unevaluated Populations

The safety and efficacy of ZYCLARA Cream have not been established in the treatment of:
- urethral, intra-vaginal, cervical, rectal or intra-anal human papilloma viral disease.
- actinic keratosis when treated with more than one 2-cycle treatment course in the same area.
- patients with xeroderma pigmentosum.
- superficial basal cell carcinoma.
- immunosuppressed patients.

CONTRAINDICATIONS None.

WARNINGS AND PRECAUTIONS

Local Skin Reactions

Intense local skin reactions including skin weeping or erosion can occur after a few applications of ZYCLARA Cream and may require an interruption of dosing. ZYCLARA Cream has the potential to exacerbate inflammatory conditions of the skin, including chronic graft versus host disease.

Administration of ZYCLARA Cream is not recommended until the skin is healed from any previous drug or surgical treatment.

Systemic Reactions

Flu-like signs and symptoms may accompany, or even precede, local skin reactions and may include fatigue, nausea, fever, myalgias, arthralgias, malaise and chills. An interruption of dosing and assessment of the patient should be considered.

Lymphadenopathy occurred in 2% of subjects with actinic keratosis treated with ZYCLARA Cream. This reaction resolved in all subjects by 4 weeks after completion of treatment.

Ultraviolet Light Exposure Risks

Exposure to sunlight (including sunlamps) should be avoided or minimized during use of ZYCLARA Cream. Patients should be warned to use protective clothing (e.g., a hat) when using ZYCLARA Cream. Patients with sunburn should be advised not to use ZYCLARA Cream until fully recovered. Patients who may have considerable sun exposure, e.g. due to their occupation, and those patients with inherent sensitivity to sunlight should exercise caution when using ZYCLARA Cream.

In an animal photo-carcinogenicity study, imiquimod cream shortened the time to skin tumor formation. The enhancement of ultraviolet carcinogenicity is not necessarily dependent on phototoxic mechanisms. Therefore, patients should minimize or avoid natural or artificial sunlight exposure.

Increased Risk of Adverse Reactions with Concomitant Imiquimod Use

Concomitant use of ZYCLARA and any other imiquimod products, in the same treatment area, should be avoided since they contain the same active ingredient (imiquimod) and may increase the risk for and severity of local skin reactions.

The safety of concomitant use of ZYCLARA Cream and any other imiquimod products has not been established and should be avoided since they contain the same active ingredient (imiquimod) and may increase the risk for and severity of systemic reactions.

Immune Cell Activation in Autoimmune Disease

ZYCLARA Cream should be used with caution in patients with pre-existing autoimmune conditions because imiquimod activates immune cells.

ADVERSE REACTIONS

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Clinical Trials Experience: External Genital Warts

In two double-blind, placebo-controlled studies 602 subjects applied up to one packet of ZYCLARA Cream or vehicle daily for up to 8 weeks.

The most frequently reported adverse reactions were application site reactions and local skin reactions. Selected adverse reactions are listed in Table 1.

Table 1: Selected Adverse Reactions Occurring in ≥2% of ZYCLARA Treated Subjects and at a Greater Frequency than with Vehicle in the Combined Trials (EGW)

Preferred Term	ZYCLARA Cream 3.75% (N=400)	Vehicle Cream (N=202)
Application site pain	28 (7%)	1 (<1%)
Application site irritation	24 (6%)	2 (1%)
Application site pruritus	11 (3%)	2 (1%)
Vaginitis bacterial*	6 (3%)	2 (2%)
Headache	6 (2%)	1 (<1%)

*Percentage based on female population of 6/216 for ZYCLARA Cream 3.75% and 2/106 for vehicle cream

Local skin reactions were recorded as adverse reactions only if they extended beyond the treatment area, if they required any medical intervention, or they resulted in patient discontinuation from the study. The incidence and severity of selected local skin reactions are shown in Table 2.

Table 2: Selected Local Skin Reactions in the Treatment Area Assessed by the Investigator (EGW)

All grades*, (%)	Severe, (%)	ZYCLARA Cream 3.75% (N=400)	Vehicle Cream (N=202)
Erythema*		70%	27%
	Severe erythema	9%	<1%
Edema*		41%	8%
	Severe edema	2%	0%
Erosion/ulceration*		36%	4%
	Severe erosion/ulceration	11%	<1%
Exudate*		34%	2%
	Severe exudate	2%	0%

*Mild, Moderate, or Severe

The frequency and severity of local skin reactions were similar in both genders, with the following exceptions: a) flaking/scaling occurred in 40% of men and in 26% of women and b) scabbing/crusting occurred in 34% of men and in 18% of women.

In the clinical trials, 32% (126/400) of subjects who used ZYCLARA Cream and 2% (4/202) of subjects who used vehicle cream discontinued treatment temporarily (required rest periods) due to adverse local skin reactions, and 1% (3/400) of subjects who used ZYCLARA Cream discontinued treatment permanently due to local skin/application site reactions.

Other adverse reactions reported in subjects treated with ZYCLARA Cream include: rash, back pain, application site rash, application site cellulitis, application site excoriation, application site bleeding, scrotal pain, scrotal erythema, scrotal ulcer, scrotal edema, sinusitis, nausea, pyrexia, and influenza-like symptoms.

Postmarketing Experience

The following adverse reactions have been identified during post-approval use of imiquimod. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Application Site Disorders: tingling at the application site.

Body as a Whole: angioedema.

Cardiovascular: capillary leak syndrome, cardiac failure, cardiomyopathy, pulmonary edema, arrhythmias (tachycardia, supraventricular tachycardia, atrial fibrillation, palpitations), chest pain, ischemia, myocardial infarction, syncope.

Endocrine: thyroiditis.

Gastro-Intestinal System Disorders: abdominal pain.

Hematological: decreases in red cell, white cell and platelet counts (including idiopathic thrombocytopenic purpura), lymphoma.

Hepatic: abnormal liver function.

Infections and Infestations: herpes simplex.

Musculo-Skeletal System Disorders: arthralgia.

Neuropsychiatric: agitation, cerebrovascular accident, convulsions (including febrile convulsions), depression, insomnia, multiple sclerosis aggravation, paresis, suicide.

Respiratory: dyspnea.

Urinary System Disorders: proteinuria, urinary retention, dysuria.

Skin and Appendages: exfoliative dermatitis, erythema multiforme, hyperpigmentation, hypertrophic scar, hypopigmentation.

Vascular: Henoch-Schonlein purpura syndrome.

USE IN SPECIFIC POPULATIONS

Pregnancy Pregnancy Category C:

There are no adequate and well-controlled studies in pregnant women. ZYCLARA Cream should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

The animal multiples of human exposure calculations were based on daily dose comparisons for the reproductive toxicology studies described in this label. The animal multiples of human exposure were based on weekly dose comparisons for the carcinogenicity studies described in this label. For the animal multiple of human exposure ratios presented in this label, the Maximum Recommended Human Dose (MRHD) was set at 2 packets (500 mg cream) per treatment of actinic keratosis with ZYCLARA Cream (imiquimod 3.75%, 18.75 mg imiquimod) for BSA comparison. The maximum human AUC value obtained in the treatment of external genital and perianal warts was higher than that obtained in the treatment of actinic keratosis and was used in the calculation of animal multiples of MRHD that were based on AUC comparison.

Systemic embryofetal development studies were conducted in rats and rabbits. Oral doses of 1, 5 and 20 mg/kg/day imiquimod were administered during the period of organogenesis (gestational days 6 – 15) to pregnant female rats. In the presence of maternal toxicity, fetal effects noted at 20 mg/kg/day (163X MRHD based on AUC comparisons) included increased resorptions, decreased fetal body weights, delays in skeletal ossification, bent limb bones, and two fetuses in one litter (2 of 1567 fetuses) demonstrated exencephaly, protruding tongues and low-set ears. No treatment related effects on embryofetal toxicity or teratogenicity were noted at 5 mg/kg/day (28X MRHD based on AUC comparisons).

Intravenous doses of 0.5, 1 and 2 mg/kg/day imiquimod were administered during the period of organogenesis (gestational days 6 – 18) to pregnant female rabbits. No treatment related effects on embryofetal toxicity or teratogenicity were noted at 2 mg/kg/day (2.1X MRHD based on BSA comparisons), the highest dose evaluated in this study, or 1 mg/kg/day (115X MRHD based on AUC comparisons).

A combined fertility and peri- and post-natal development study was conducted in rats. Oral doses of 1, 1.5, 3 and 6 mg/kg/day imiquimod were administered to male rats from 70 days prior to mating through the mating period and to female rats from 14 days prior to mating through parturition and lactation. No effects on growth, fertility, reproduction or post-natal development were noted at doses up to 6 mg/kg/day (25X MRHD based on AUC comparisons), the highest dose evaluated in this study. In the absence of maternal toxicity, bent limb bones were noted in the F1 fetuses at a dose of 6 mg/kg/day (25X MRHD based on AUC comparisons). This fetal effect was also noted in the oral rat embryofetal development study conducted with imiquimod. No treatment related effects on teratogenicity were noted at 3 mg/kg/day (12X MRHD based on AUC comparisons).

Nursing Mothers

It is not known whether imiquimod is excreted in human milk following use of ZYCLARA Cream. Because many drugs are excreted in human milk, caution should be exercised when ZYCLARA Cream is administered to nursing women.

Pediatric Use

Safety and efficacy in patients with external genital/perianal warts below the age of 12 years have not been established.

Geriatric Use

Clinical studies of ZYCLARA Cream for EGW did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Of the 400 subjects treated with ZYCLARA Cream in the EGW clinical studies, 5 subjects (1%) were 65 years or older.

OVERDOSAGE

Topical overdosing of ZYCLARA Cream could result in an increased incidence of severe local skin reactions and may increase the risk for systemic reactions.

Hypotension was reported in a clinical trial following multiple oral imiquimod doses of >200 mg (equivalent to ingestion of the imiquimod content of more than 21 packets of ZYCLARA). The hypotension resolved following oral or intravenous fluid administration.

Rx Only

GRACEWAY® PHARMACEUTICALS

Manufactured by
3M Health Care Limited
Loughborough LE11 1EP England

Distributed by
Graceway Pharmaceuticals, LLC
Bristol, TN 37620

Issued: March 2011
ZYC031137

Po# 4500010169. 560028 2 ✓

SH Media, LLC
11 Rose Meadow Way
Aquinnah, MA 02535
508-645-9022

Cmb

INSERTION ORDER

To: Dominic Barone Date: 9/8/11

Fax No.: 646-638-6120 Insertion Order No.: GRW11126

Tel No.: 646-638-6097

From: Stefanie Hecht 508-645-9022, 508-645-9021 Fax

For Insertion In: JAAPA

CLIENT:	Graceway Pharmaceuticals
PRODUCT:	ZYCLARA
DATE OF ISSUE:	October
AD UNIT:	Page 4CB + Page BW
AD NO.:	ZYC1110188
HEADLINE:	"Thwarted"
POSITION:	Far forward
TIME RATE - SPACE:	48x
COLOR:	1x
NET COST:	$8,321.50
MATERIAL FROM:	Repeat from September
SPECIAL INSTRUCTIONS:	

provisional calculation
Gross:
Net:

NAME DATE

Please send invoices to: Graceway Pharmaceuticals, Attn: Accounts Payable, 340 Martin Luther King Jr Blvd, Suite 400, Bristol, TN 37620

IF INCLUDED, PRESCRIBING INFORMATION MUST RUN IMMEDIATELY ADJACENT TO AD

PLEASE SEND TWO (2) TEAR SHEETS ALONG WITH INVOICE

HAYMARKET MEDIA INC.

114 West 26th Street - 3rd Floor
New York, NY 10001
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INVOICE

ACCOUNTS PAYABLES
GRACEWAY PHARMACEUTICALS
340 MARTIN LUTHER KING BLVD.
SUITE 400, BRISTOL, TN
37620

Invoice No:	JA102011
Date:	09/08/11
Your Order Ref :	GRW11127
Account No :	560628

Description		Value
Your Client:	**Graceway Pharmaceuticals**	
Publication:	**JAAPA**	
		8,321.50
Cover Date :	01-October-2011	
Your Contact:	Accounts Payables	
Our Salesperson:	Dominic Barone	
	PO #4500010169	
Product:	Zyclara	
Frequency Rate:	48	
Page Number/s:	29, 30	
		8,321.50
	Net Value	8,321.50

REMITTANCE RECORD

Customer :	GRACEWAY PHARMACEUTICALS	**Payment Terms**	Net 30 Days
Account No :	560628	**Due Date**	**10/07/11**
Invoice No :	46605	**Total Due** USD	8,321.50

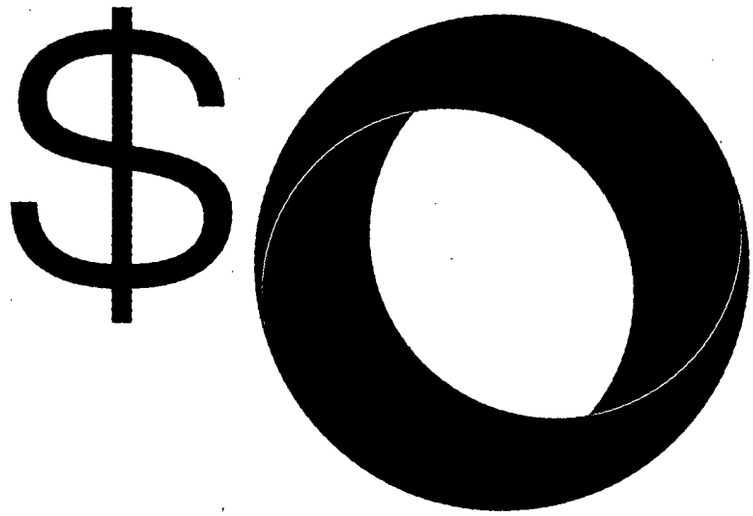
Amount Enclosed $

Cheque Number

Please make all cheques payable to **Haymarket Media, Inc. PO BOX 512368, Philadelphia, PA 19175-2368** and remit to this address with this bottom portion of the invoice. Thank You.

In the treatment of actinic keratosis

What will your patients pay for significant lesion reduction?



The Zyclara Zero Program

Zyclara Patient Savings Card

RxBIN: 610524
RxPCN: Loyalty
RxGRP: 50775525
ISSUER: (80840)
ID: 01234567

Zyclara (imiquimod) Cream 3.75%

Powered By: McKESSON Empowering Healthcare

GRACEWAY PHARMACEUTICALS, LLC

Most card holders pay $0 per prescription

- Maximum benefit of $300 per use
- Limit of 2 uses per card; some restrictions apply*

Zyclara® (imiquimod) Cream 3.75%

- 36% of patients had complete clearance vs 6% for placebo ($P<.001$)[1]
- 59% had partial clearance vs 23% for placebo ($P<.001$)[1]

Zyclara Cream is indicated for the topical treatment of clinically typical visible or palpable actinic keratoses (AK) of the full face or balding scalp in immunocompetent adults.

In clinical studies, the most common side effects involved skin reactions in the application area. These reactions included erythema, scabbing or crusting, flaking, scaling or dryness, edema, erosion or ulceration, and weeping or exudate. Most skin reactions were rated as mild to moderate. Intense local inflammatory reactions and/or flu-like systemic signs and symptoms can occur. Dosing interruptions may be required.

Exposure to natural or artificial sunlight (tanning beds or UVA/B treatment) should be avoided or minimized during use of Zyclara Cream.

Please see Brief Summary of Full Prescribing Information on adjacent page.

Visit us at **www.ZyclaraCream.com**

*Patient not eligible if any one of the following apply: (1) prescriptions are paid in part or full by any state or federally funded programs including but not limited to Medicare or Medicaid, Medigap, VA, DOD, or TriCare; (2) patient does not have any prescription drug benefits; (3) patient is a resident of MA; (4) where prohibited by law; (5) patient is under the age of 18. LoyaltyScript® is not an insurance card.

For questions regarding setup, claim transmission, patient eligibility, or other issues, call the ZYCLARA Patient Savings Card Program at 1-877-264-2440 (8:00 AM through 8:00 PM EST, Monday through Friday).

Reference: 1. Swanson N, Abramovits W, Berman B, et al. Imiquimod 2.5% and 3.75% for the treatment of actinic keratoses: results of 2 placebo-controlled studies of daily application to the face and balding scalp for two 2-week cycles. *J Am Acad Dermatol.* 2010;62(4):582-590.

GRACEWAY® PHARMACEUTICALS

Zyclara™ [zi-clar-a]
(imiquimod) Cream 3.75%

BRIEF SUMMARY OF PRESCRIBING INFORMATION

SEE PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

INDICATIONS AND USAGE

Actinic Keratosis

ZYCLARA Cream is indicated for the topical treatment of clinically typical visible or palpable actinic keratoses (AK), of the full face or balding scalp in immunocompetent adults.

Unevaluated Populations

Safety and efficacy have not been established for ZYCLARA Cream in the treatment of actinic keratosis, with more than one 2-cycle treatment course in the same area.

The safety and efficacy of ZYCLARA Cream in immunosuppressed patients have not been established.

The safety and efficacy have not been established for ZYCLARA Cream in the treatment of patients with xeroderma pigmentosum.

The safety and efficacy have not been established for ZYCLARA Cream in the treatment of superficial basal cell carcinoma.

The safety and efficacy have not been established for ZYCLARA Cream in the treatment of external genital warts.

ZYCLARA Cream should be used with caution in patients with pre-existing autoimmune conditions.

CONTRAINDICATIONS

None (4)

WARNINGS AND PRECAUTIONS

Local Skin Reactions

Intense local skin reactions including skin weeping or erosion can occur after a few applications of ZYCLARA Cream and may require an interruption of dosing. *[see Dosage and Administration (2) and Adverse Reactions (6)]*. ZYCLARA Cream has the potential to exacerbate inflammatory conditions of the skin, including chronic graft versus host disease.

Administration of ZYCLARA Cream is not recommended until the skin is healed from any previous drug or surgical treatment.

Concomitant use of ZYCLARA and any other imiquimod creams, in the same treatment area, should be avoided since they contain the same active ingredient (imiquimod) and may increase the risk for and severity of local skin reactions.

Systemic Reactions

Flu-like signs and symptoms may accompany, or even precede, local skin reactions and may include fatigue, nausea, fever, myalgias, arthralgias, and chills. An interruption of dosing and an assessment of the patient should be considered. *[see Adverse Reactions (6)]*

Lymphadenopathy occurred in 2% of subjects treated with ZYCLARA Cream *[see Adverse Reactions (6)]*. This reaction resolved in all subjects by 4 weeks after completion of treatment.

The safety of concomitant use of ZYCLARA Cream and any other imiquimod creams has not been established and should be avoided since they contain the same active ingredient (imiquimod) and may increase the risk for and severity of systemic reactions.

Ultraviolet Light Exposure

Exposure to sunlight (including sunlamps) should be avoided or minimized during use of ZYCLARA Cream because of concern for heightened sunburn susceptibility. Patients should be warned to use protective clothing (e.g., a hat) when using ZYCLARA Cream. Patients with sunburn should be advised not to use ZYCLARA Cream until fully recovered. Patients who may have considerable sun exposure, e.g., due to their occupation, and those patients with inherent sensitivity to sunlight should exercise caution when using ZYCLARA Cream.

In an animal photo-carcinogenicity study, imiquimod cream shortened the time to skin tumor formation *[see Nonclinical Toxicology (13.1)]*. The enhancement of ultraviolet carcinogenicity is not necessarily dependent on phototoxic mechanisms. Therefore, patients should minimize or avoid natural or artificial sunlight exposure.

ADVERSE REACTIONS

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Clinical Trials Experience

The data described below reflect exposure to ZYCLARA Cream or placebo in 319 subjects enrolled in two double-blind, vehicle-controlled studies. Subjects applied up to two packets of ZYCLARA Cream or vehicle daily to the skin of the affected area (either entire face or balding scalp) for two 2-week treatment cycles separated by a 2-week no-treatment period.

Table 1: Selected Adverse Reactions Occurring in ≥2% of ZYCLARA-Treated Subjects and at a Greater Frequency Than With Vehicle in the Combined Studies

Preferred Term	ZYCLARA Cream 3.75% (N=160)	Vehicle (N=159)
Headache	10 (6%)	5 (3%)
Application site pruritus	7 (4%)	1 (<1%)
Fatigue	7 (4%)	0 (0%)
Nausea	6 (3%)	2 (1%)
Application site irritation	5 (3%)	0 (0%)
Application site pain	5 (3%)	0 (0%)
Pyrexia	5 (3%)	0 (0%)
Anorexia	4 (3%)	0 (0%)
Dizziness	4 (3%)	0 (0%)
Herpes simplex	4 (3%)	1 (<1%)
Pain	4 (3%)	0 (0%)
Chest pain	3 (2%)	0 (0%)
Diarrhea	3 (2%)	0 (0%)
Lymphadenopathy	3 (2%)	0 (0%)

Table 2: Local Skin Reactions in the Treatment Area in ZYCLARA-Treated Subjects as Assessed by the Investigator

	ZYCLARA Cream 3.75% (n=160)		Vehicle (n=159)	
	All Grades*	Severe	All Grades*	Severe
Erythema	154 (96%)	40 (25%)	124 (78%)	0 (0%)
Scabbing/Crusting	149 (93%)	22 (14%)	72 (45%)	0 (0%)
Flaking/Scaling/Dryness	147 (92%)	13 (8%)	123 (77%)	2 (1%)
Edema	120 (75%)	9 (6%)	31 (19%)	0 (0%)
Erosion/Ulceration	99 (62%)	17 (11%)	14 (9%)	0 (0%)
Weeping/Exudate	81 (51%)	9 (6%)	6 (4%)	0 (0%)

*All Grades: mild, moderate or severe

Local skin reactions may extend beyond treatment area.

Overall, in the clinical trials, 11% (17/160) of subjects on ZYCLARA Cream and 0% on vehicle cream required rest periods due to adverse reactions.

Other adverse reactions observed in subjects treated with ZYCLARA Cream include: application site bleeding, application site swelling, arthralgia, cheilitis, chills, dermatitis, herpes zoster, influenza-like illness, insomnia, lethargy, myalgia, pancytopenia, pruritus, squamous cell carcinoma, and vomiting.

Postmarketing Experience

There are currently no postmarketing adverse reactions reported for ZYCLARA Cream.

The following adverse reactions have been identified during post-approval use of Aldara (imiquimod) Cream, 5%. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Body as a Whole: angioedema.

Cardiovascular: capillary leak syndrome, cardiac failure, cardiomyopathy, pulmonary edema, arrhythmias (tachycardia, supraventricular tachycardia, atrial fibrillation, palpitations), chest pain, ischemia, myocardial infarction, syncope.

Endocrine: thyroiditis.

Gastro-Intestinal System Disorders: abdominal pain.

Hematological: decreases in red cell, white cell and platelet counts (including idiopathic thrombocytopenic purpura), lymphoma.

Hepatic: abnormal liver function.

Infections and Infestations: herpes simplex.

Neuropsychiatric: agitation, cerebrovascular accident, convulsions (including febrile convulsions), depression, insomnia, multiple sclerosis aggravation, paresis, suicide.

Respiratory: dyspnea.

Urinary System Disorders: proteinuria, urinary retention, dysuria.

Skin and Appendages: exfoliative dermatitis, erythema multiforme, hyperpigmentation, hypertrophic scar.

Vascular: Henoch-Schonlein purpura syndrome.

USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Category C:

There are no adequate and well-controlled studies in pregnant women. ZYCLARA Cream should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Note: The animal multiples of human exposure calculations were based on daily dose comparisons for the reproductive toxicology studies described in this label. The animal multiples of human exposure were based on weekly dose comparisons for the carcinogenicity studies described in this label. For the animal multiple of human exposure ratios presented in this label, the Maximum Recommended Human Dose (MRHD) was set at 2 packets (500 mg cream) per treatment of ZYCLARA Cream (imiquimod 3.75%, 18.75 mg imiquimod).

Systemic embryofetal development studies were conducted in rats and rabbits. Oral doses of 1, 5, and 20 mg/kg/day imiquimod were administered during the period of organogenesis (gestational days 6 – 15) to pregnant female rats. In the presence of maternal toxicity, fetal effects noted at 20 mg/kg/day (190X MRHD based on AUC comparisons) included increased resorptions, decreased fetal body weights, delays in skeletal ossification, bent limb bones, and two fetuses in one litter (2 of 1567 fetuses) demonstrated exencephaly, protruding tongues, and low-set ears. No treatment-related effects on embryofetal toxicity or teratogenicity were noted at 5 mg/kg/day (32X MRHD based on AUC comparisons).

Intravenous doses of 0.5, 1, and 2 mg/kg/day imiquimod were administered during the period of organogenesis (gestational days 6 – 18) to pregnant female rabbits. No treatment-related effects on embryofetal toxicity or teratogenicity were noted at 2 mg/kg/day (2.1X MRHD based on BSA comparisons), the highest dose evaluated in this study, or 1 mg/kg/day (134X MRHD based on AUC comparisons).

A combined fertility and peri- and post-natal development study was conducted in rats. Oral doses of 1, 1.5, 3, and 6 mg/kg/day imiquimod were administered to male rats from 70 days prior to mating through the mating period and to female rats from 14 days prior to mating through parturition and lactation. No effects on growth, fertility, reproduction, or post-natal development were noted at doses up to 6 mg/kg/day (29X MRHD based on AUC comparisons), the highest dose evaluated in this study. In the absence of maternal toxicity, bent limb bones were noted in the F1 fetuses at a dose of 6 mg/kg/day (29X MRHD based on AUC comparisons). This fetal effect was also noted in the oral rat embryofetal development study conducted with imiquimod. No treatment-related effects on teratogenicity were noted at 3 mg/kg/day (14X MRHD based on AUC comparisons).

Nursing Mothers

It is not known whether imiquimod is excreted in human milk following use of ZYCLARA Cream. Because many drugs are excreted in human milk, caution should be exercised when ZYCLARA Cream is administered to nursing women.

Pediatric Use

AK is not a condition generally seen within the pediatric population. The safety and efficacy of ZYCLARA Cream for AK in patients less than 18 years of age has not been established.

Geriatric Use

Of the 160 subjects treated with ZYCLARA Cream in the clinical studies, 78 subjects were 65 years and older. No overall differences in safety or effectiveness were observed between these subjects and younger subjects.

OVERDOSAGE

Topical overdosing of ZYCLARA Cream could result in an increased incidence of severe local skin reactions and may increase the risk for systemic reactions.

Hypotension was reported in a clinical trial following multiple oral imiquimod doses of >200 mg (equivalent to the ingestion of imiquimod content of >21 packets of ZYCLARA). This resolved following oral or intravenous fluid administration.

Rx Only

GRACEWAY® PHARMACEUTICALS

Manufactured by
3M Health Care Limited
Loughborough LE11 1EP England

Distributed by
Graceway Pharmaceuticals, LLC
Bristol, TN 37620

Issued: March 2010
ZYC0410135

560628

PO# 4500010169.

CMS

SH Media, LLC
11 Rose Meadow Way
Aquinnah, MA 02535
508-645-9022

INSERTION ORDER

To: Dominic Barone Date: 9/8/11

Fax No.: 646-638-6120 Insertion Order No.: GRW11127

Tel No.: 646-638-6097

From: Stefanie Hecht 508-645-9022, 508-645-9021 Fax

For Insertion In: JAAPA

CLIENT:	Graceway Pharmaceuticals
PRODUCT:	ZYCLARA
DATE OF ISSUE:	October
AD UNIT:	Page 4CB + Page BW
AD NO.:	ZYC0910179a
HEADLINE:	"What Will Your Patients Pay for Significant Lesion Reduction?"
POSITION:	Far forward
TIME RATE - SPACE:	48x
COLOR:	1x
NET COST:	$8,321.50
MATERIAL FROM:	Repeat from April
SPECIAL INSTRUCTIONS:	

Provisional:
Calculation:
Gross:
Net:

NAME DATE

Please send Invoices to: Graceway Pharmaceuticals, Attn: Accounts Payable, 340 Martin Luther King Jr Blvd, Suite 400, Bristol, TN 37620

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INVOICE

ACCOUNTS PAYABLES
GRACEWAY PHARMACEUTICALS
340 MARTIN LUTHER KING BLVD.
SUITE 400, BRISTOL, TN
37620

Invoice No:	JA102011A
Date:	09/08/11
Your Order Ref :	GRW11127
Account No :	560628

Description		Value
Your Client:	**Graceway Pharmaceuticals**	
Publication:	**JAAPA**	
		8,321.50
Cover Date :	01-October-2011	
Your Contact:	Accounts Payables	
Our Salesperson:	Dominic Barone	
	PO #4500010169	
Product:	Zyclara	
Frequency Rate:	48	
Page Number/s:	61, 62	
		8,321.50
	Net Value	8,321.50

REMITTANCE RECORD

Customer :	GRACEWAY PHARMACEUTICALS	**Payment Terms**	Net 30 Days
Account No :	560628	**Due Date**	**10/07/11**
Invoice No :	46605	**Total Due** USD	8,321.50

Amount Enclosed $

Cheque Number

Please make all cheques payable to **Haymarket Media, Inc. PO BOX 512368, Philadelphia, PA 19175-2368** and remit to this address with this bottom portion of the invoice. Thank You.

GENITAL WARTS

THWARTED!

Short treatment, daily dosing

- Applied once daily for up to 8 weeks[1]

Significant clearance of external genital warts[1]

In females–

- 37% complete clearance; 48% partial clearance

In males–

- 19% complete clearance; 27% partial clearance
  – Partial clearance defined as ≥75% reduction in EGW count from baseline

Many patients who cleared with Zyclara remained clear[1]

- Only 15% of patients had a recurrence at 12 weeks posttreatment

Tough on warts, easy on patients

- Low incidence of treatment-related adverse events at the application site: itching (3%), irritation (6%), or pain (7%)[1]
- Local skin reactions, most of which were mild to moderate, included severe erythema (9%) and severe erosion/ulceration (11%)[1]

Zyclara®
(imiquimod) Cream
3.75%

Zyclara Cream is indicated for the treatment of external genital and perianal warts/condyloma acuminata in patients 12 years or older.

In clinical studies, the most frequently reported adverse reactions were local skin and application site reactions. These reactions included erythema, edema, erosion or ulceration, and exudate at the genital wart site. Most local skin reactions were rated as mild to moderate. Intense local inflammatory reactions and/or flu-like systemic signs and symptoms can occur. Dosing interruptions may be required.

Avoid concomitant use of Zyclara Cream and any other imiquimod cream because of increased risk for adverse reactions.

Zyclara Cream is not recommended for the treatment of urethral, intra-vaginal, cervical, rectal, or intra-anal human papilloma viral disease as it has not been studied.

The effect of Zyclara Cream on the transmission of genital warts is unknown. Zyclara Cream may weaken condoms and diaphragms. Sexual contact should be avoided while the cream is on the skin.

Please see Brief Summary of Prescribing Information on adjacent page.

Reference: 1. Data on file, Graceway Pharmaceuticals, LLC.

Zyclara® [zi-clar-a]
(imiquimod) Cream 3.75%

BRIEF SUMMARY OF PRESCRIBING INFORMATION

SEE PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

INDICATIONS AND USAGE

External Genital Warts

ZYCLARA Cream is indicated for the treatment of external genital and perianal warts (EGW)/condyloma acuminata in patients 12 years or older.

Limitations of Use

Treatment with ZYCLARA has not been studied for prevention or transmission of HPV.

Unevaluated Populations

The safety and efficacy of ZYCLARA Cream have not been established in the treatment of:
- urethral, intra-vaginal, cervical, rectal or intra-anal human papilloma viral disease.
- actinic keratosis when treated with more than one 2-cycle treatment course in the same area.
- patients with xeroderma pigmentosum.
- superficial basal cell carcinoma.
- immunosuppressed patients.

CONTRAINDICATIONS None.

WARNINGS AND PRECAUTIONS

Local Skin Reactions

Intense local skin reactions including skin weeping or erosion can occur after a few applications of ZYCLARA Cream and may require an interruption of dosing. ZYCLARA Cream has the potential to exacerbate inflammatory conditions of the skin, including chronic graft versus host disease.

Administration of ZYCLARA Cream is not recommended until the skin is healed from any previous drug or surgical treatment.

Systemic Reactions

Flu-like signs and symptoms may accompany, or even precede, local skin reactions and may include fatigue, nausea, fever, myalgias, arthralgias, malaise and chills. An interruption of dosing and assessment of the patient should be considered.

Lymphadenopathy occurred in 2% of subjects with actinic keratosis treated with ZYCLARA Cream. This reaction resolved in all subjects by 4 weeks after completion of treatment.

Ultraviolet Light Exposure Risks

Exposure to sunlight (including sunlamps) should be avoided or minimized during use of ZYCLARA Cream. Patients should be warned to use protective clothing (e.g., a hat) when using ZYCLARA Cream. Patients with sunburn should be advised not to use ZYCLARA Cream until fully recovered. Patients who may have considerable sun exposure, e.g. due to their occupation, and those patients with inherent sensitivity to sunlight should exercise caution when using ZYCLARA Cream.

In an animal photo-carcinogenicity study, imiquimod cream shortened the time to skin tumor formation. The enhancement of ultraviolet carcinogenicity is not necessarily dependent on phototoxic mechanisms. Therefore, patients should minimize or avoid natural or artificial sunlight exposure.

Increased Risk of Adverse Reactions with Concomitant Imiquimod Use

Concomitant use of ZYCLARA and any other imiquimod products, in the same treatment area, should be avoided since they contain the same active ingredient (imiquimod) and may increase the risk for and severity of local skin reactions.

The safety of concomitant use of ZYCLARA Cream and any other imiquimod products has not been established and should be avoided since they contain the same active ingredient (imiquimod) and may increase the risk for and severity of systemic reactions.

Immune Cell Activation in Autoimmune Disease

ZYCLARA Cream should be used with caution in patients with pre-existing autoimmune conditions because imiquimod activates immune cells.

ADVERSE REACTIONS

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Clinical Trials Experience: External Genital Warts

In two double-blind, placebo-controlled studies 602 subjects applied up to one packet of ZYCLARA Cream or vehicle daily for up to 8 weeks.

The most frequently reported adverse reactions were application site reactions and local skin reactions. Selected adverse reactions are listed in Table 1.

Table 1: Selected Adverse Reactions Occurring in ≥2% of ZYCLARA Treated Subjects and at a Greater Frequency than with Vehicle in the Combined Trials (EGW)

Preferred Term	ZYCLARA Cream 3.75% (N=400)	Vehicle Cream (N=202)
Application site pain	28 (7%)	1 (<1%)
Application site irritation	24 (6%)	2 (1%)
Application site pruritus	11 (3%)	2 (1%)
Vaginitis bacterial*	6 (3%)	2 (2%)
Headache	6 (2%)	1 (<1%)

*Percentage based on female population of 6/216 for ZYCLARA Cream 3.75% and 2/106 for vehicle cream

Local skin reactions were recorded as adverse reactions only if they extended beyond the treatment area, if they required any medical intervention, or they resulted in patient discontinuation from the study. The incidence and severity of selected local skin reactions are shown in Table 2.

Table 2: Selected Local Skin Reactions in the Treatment Area Assessed by the Investigator (EGW)

All grades*, (%)	Severe, (%)	ZYCLARA Cream 3.75% (N=400)	Vehicle Cream (N=202)
Erythema*		70%	27%
	Severe erythema	9%	<1%
Edema*		41%	8%
	Severe edema	2%	0%
Erosion/ulceration*		36%	4%
	Severe erosion/ulceration	11%	<1%
Exudate*		34%	2%
	Severe exudate	2%	0%

*Mild, Moderate, or Severe

The frequency and severity of local skin reactions were similar in both genders, with the following exceptions: a) flaking/scaling occurred in 40% of men and in 26% of women and b) scabbing/crusting occurred in 34% of men and in 18% of women.

In the clinical trials, 32% (126/400) of subjects who used ZYCLARA Cream and 2% (4/202) of subjects who used vehicle cream discontinued treatment temporarily (required rest periods) due to adverse local skin reactions, and 1% (3/400) of subjects who used ZYCLARA Cream discontinued treatment permanently due to local skin/application site reactions.

Other adverse reactions reported in subjects treated with ZYCLARA Cream include: rash, back pain, application site rash, application site cellulitis, application site excoriation, application site bleeding, scrotal pain, scrotal erythema, scrotal ulcer, scrotal edema, sinusitis, nausea, pyrexia, and influenza-like symptoms.

Postmarketing Experience

The following adverse reactions have been identified during post-approval use of imiquimod. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Application Site Disorders: tingling at the application site.

Body as a Whole: angioedema.

Cardiovascular: capillary leak syndrome, cardiac failure, cardiomyopathy, pulmonary edema, arrhythmias (tachycardia, supraventricular tachycardia, atrial fibrillation, palpitations), chest pain, ischemia, myocardial infarction, syncope.

Endocrine: thyroiditis.

Gastro-Intestinal System Disorders: abdominal pain.

Hematological: decreases in red cell, white cell and platelet counts (including idiopathic thrombocytopenic purpura), lymphoma.

Hepatic: abnormal liver function.

Infections and Infestations: herpes simplex.

Musculo-Skeletal System Disorders: arthralgia.

Neuropsychiatric: agitation, cerebrovascular accident, convulsions (including febrile convulsions), depression, insomnia, multiple sclerosis aggravation, paresis, suicide.

Respiratory: dyspnea.

Urinary System Disorders: proteinuria, urinary retention, dysuria.

Skin and Appendages: exfoliative dermatitis, erythema multiforme, hyperpigmentation, hypertrophic scar, hypopigmentation.

Vascular: Henoch-Schonlein purpura syndrome.

USE IN SPECIFIC POPULATIONS

Pregnancy Pregnancy Category C:

There are no adequate and well-controlled studies in pregnant women. ZYCLARA Cream should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

The animal multiples of human exposure calculations were based on daily dose comparisons for the reproductive toxicology studies described in this label. The animal multiples of human exposure were based on weekly dose comparisons for the carcinogenicity studies described in this label. For the animal multiple of human exposure ratios presented in this label, the Maximum Recommended Human Dose (MRHD) was set at 2 packets (500 mg cream) per treatment of actinic keratosis with ZYCLARA Cream (imiquimod 3.75%, 18.75 mg imiquimod) for BSA comparison. The maximum human AUC value obtained in the treatment of external genital and perianal warts was higher than that obtained in the treatment of actinic keratosis and was used in the calculation of animal multiples of MRHD that were based on AUC comparison.

Systemic embryofetal development studies were conducted in rats and rabbits. Oral doses of 1, 5 and 20 mg/kg/day imiquimod were administered during the period of organogenesis (gestational days 6 – 15) to pregnant female rats. In the presence of maternal toxicity, fetal effects noted at 20 mg/kg/day (163X MRHD based on AUC comparisons) included increased resorptions, decreased fetal body weights, delays in skeletal ossification, bent limb bones, and two fetuses in one litter (2 of 1567 fetuses) demonstrated exencephaly, protruding tongues and low-set ears. No treatment related effects on embryofetal toxicity or teratogenicity were noted at 5 mg/kg/day (28X MRHD based on AUC comparisons).

Intravenous doses of 0.5, 1 and 2 mg/kg/day imiquimod were administered during the period of organogenesis (gestational days 6 – 18) to pregnant female rabbits. No treatment related effects on embryofetal toxicity or teratogenicity were noted at 2 mg/kg/day (2.1X MRHD based on BSA comparisons), the highest dose evaluated in this study, or 1 mg/kg/day (115X MRHD based on AUC comparisons).

A combined fertility and peri- and post-natal development study was conducted in rats. Oral doses of 1, 1.5, 3 and 6 mg/kg/day imiquimod were administered to male rats from 70 days prior to mating through the mating period and to female rats from 14 days prior to mating through parturition and lactation. No effects on growth, fertility, reproduction or post-natal development were noted at doses up to 6 mg/kg/day (25X MRHD based on AUC comparisons), the highest dose evaluated in this study. In the absence of maternal toxicity, bent limb bones were noted in the F1 fetuses at a dose of 6 mg/kg/day (25X MRHD based on AUC comparisons). This fetal effect was also noted in the oral rat embryofetal development study conducted with imiquimod. No treatment related effects on teratogenicity were noted at 3 mg/kg/day (12X MRHD based on AUC comparisons).

Nursing Mothers

It is not known whether imiquimod is excreted in human milk following use of ZYCLARA Cream. Because many drugs are excreted in human milk, caution should be exercised when ZYCLARA Cream is administered to nursing women.

Pediatric Use

Safety and efficacy in patients with external genital/perianal warts below the age of 12 years have not been established.

Geriatric Use

Clinical studies of ZYCLARA Cream for EGW did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Of the 400 subjects treated with ZYCLARA Cream in the EGW clinical studies, 5 subjects (1%) were 65 years or older.

OVERDOSAGE

Topical overdosing of ZYCLARA Cream could result in an increased incidence of severe local skin reactions and may increase the risk for systemic reactions.

Hypotension was reported in a clinical trial following multiple oral imiquimod doses of >200 mg (equivalent to ingestion of the imiquimod content of more than 21 packets of ZYCLARA). The hypotension resolved following oral or intravenous fluid administration.

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GRACEWAY® PHARMACEUTICALS

Manufactured by
3M Health Care Limited
Loughborough LE11 1EP England

Distributed by
Graceway Pharmaceuticals, LLC
Bristol, TN 37620

Issued: March 2011
ZYC031137

Metaphor, Inc
119 Cherry Hill Road
Parsippany, NJ 07054
973-334-1009

INSERTION ORDER

560628

To: Marlis Miller

Date: 4/22/11

Fax No.: 610-454-0698

Insertion Order No.: GRW11068

Tel No.: 610-454-0643

PO#: ZYC-

From: Stefanie Hecht 508-645-9022, 508-645-9021 Fax

For Insertion In: MONTHLY PRESCRIBING REFERENCE FOR NP/PAs

CLIENT:	Graceway Pharmaceuticals
PRODUCT:	Zyclara
DATE OF ISSUE:	Summer
AD UNIT:	Page 4CB + Page BW
AD NO.:	ZYC031142
HEADLINE:	"Thwarted"
POSITION:	Far forward
TIME RATE - SPACE:	60x
COLOR:	1x
NET COST:	$12,853.28 ($250/page discount w/Clinical Advisor, 15% discount w/MPR OBG edition)
MATERIAL FROM:	New Materials
SPECIAL INSTRUCTIONS:	If materials do not arrive please contact Kathy Heffernan at 973-334-1009 or kheff@metaphorinc.com

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METAPHOR INC.
119 CHERRY HILL ROAD
PARSIPPANY, NJ, 07054

Invoice No:	45550
Date:	05/24/11
Your Order Ref :	GRW11068
Account No :	540024

Description		Value
Your Client:		
Publication:	**PANP**	
		5,519.90
Details:	Display	
Cover Date :	01-May-2011	
		7,333.38
Details:	Display	
Cover Date :	01-May-2011	
Your Contact:	Heffernan Kathleen	
Our Salesperson:	Marlis Miller	
Our Booking Ref:	0000099085	
Product:	Zyclara	
Frequency Rate:	60	
Page Number/s:	A25-A26	
		12,853.28
	Net Value	12,853.28

REMITTANCE RECORD

Customer :	METAPHOR INC.
Account No :	540024
Invoice No :	45550

Payment Terms		Net 30 Days
Due Date		**06/23/11**
Total Due	USD	12,853.28

Amount Enclosed $

Cheque Number

Please make all cheques payable to **Haymarket Media, Inc. PO BOX 512368, Philadelphia, PA 19175-2368** and remit to this address with this bottom portion of the invoice. Thank You.

GENITAL WARTS

THWARTED!

Short treatment, daily dosing

- Applied once daily for up to 8 weeks[1]

Significant clearance of external genital warts[1]

In females–

- 37% complete clearance; 48% partial clearance

In males–

- 19% complete clearance; 27% partial clearance

– Partial clearance defined as ≥75% reduction in EGW count from baseline

Many patients who cleared with Zyclara remained clear[1]

- Only 15% of patients had a recurrence at 12 weeks posttreatment

Tough on warts, easy on patients

- Low incidence of treatment-related adverse events at the application site: itching (3%), irritation (6%), or pain (7%)[1]
- Local skin reactions, most of which were mild to moderate, included severe erythema (9%) and severe erosion/ulceration (11%)[1]

Zyclara®
(imiquimod) Cream
3.75%

---

yclara Cream is indicated for the treatment of external genital and perianal warts/condyloma acuminata in patients 12 years r older.

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void concomitant use of Zyclara Cream and any other imiquimod cream because of increased risk for adverse reactions.

yclara Cream is not recommended for the treatment of urethral, intra-vaginal, cervical, rectal, or intra-anal human papilloma ral disease as it has not been studied.

he effect of Zyclara Cream on the transmission of genital warts is unknown. Zyclara Cream may weaken condoms and aphragms. Sexual contact should be avoided while the cream is on the skin.

ease see Brief Summary of Prescribing Information on adjacent page.

ference: 1. Data on file, Graceway Pharmaceuticals, LLC.

GRACEWAY® PHARMACEUTICALS

Zyclara® [zi-clar-a]
(imiquimod) Cream 3.75%

BRIEF SUMMARY OF PRESCRIBING INFORMATION

SEE PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

INDICATIONS AND USAGE

External Genital Warts

ZYCLARA Cream is indicated for the treatment of external genital and perianal warts (EGW)/condyloma acuminata in patients 12 years or older.

Limitations of Use

Treatment with ZYCLARA has not been studied for prevention or transmission of HPV.

Unevaluated Populations

The safety and efficacy of ZYCLARA Cream have not been established in the treatment of:
- urethral, intra-vaginal, cervical, rectal or intra-anal human papilloma viral disease.
- actinic keratosis when treated with more than one 2-cycle treatment course in the same area.
- patients with xeroderma pigmentosum.
- superficial basal cell carcinoma.
- immunosuppressed patients.

CONTRAINDICATIONS None.

WARNINGS AND PRECAUTIONS

Local Skin Reactions

Intense local skin reactions including skin weeping or erosion can occur after a few applications of ZYCLARA Cream and may require an interruption of dosing. ZYCLARA Cream has the potential to exacerbate inflammatory conditions of the skin, including chronic graft versus host disease.

Administration of ZYCLARA Cream is not recommended until the skin is healed from any previous drug or surgical treatment.

Systemic Reactions

Flu-like signs and symptoms may accompany, or even precede, local skin reactions and may include fatigue, nausea, fever, myalgias, arthralgias, malaise and chills. An interruption of dosing and assessment of the patient should be considered.

Lymphadenopathy occurred in 2% of subjects with actinic keratosis treated with ZYCLARA Cream. This reaction resolved in all subjects by 4 weeks after completion of treatment.

Ultraviolet Light Exposure Risks

Exposure to sunlight (including sunlamps) should be avoided or minimized during use of ZYCLARA Cream. Patients should be warned to use protective clothing (e.g., a hat) when using ZYCLARA Cream. Patients with sunburn should be advised not to use ZYCLARA Cream until fully recovered. Patients who may have considerable sun exposure, e.g. due to their occupation, and those patients with inherent sensitivity to sunlight should exercise caution when using ZYCLARA Cream.

In an animal photo-carcinogenicity study, imiquimod cream shortened the time to skin tumor formation. The enhancement of ultraviolet carcinogenicity is not necessarily dependent on phototoxic mechanisms. Therefore, patients should minimize or avoid natural or artificial sunlight exposure.

Increased Risk of Adverse Reactions with Concomitant Imiquimod Use

Concomitant use of ZYCLARA and any other imiquimod products, in the same treatment area, should be avoided since they contain the same active ingredient (imiquimod) and may increase the risk for and severity of local skin reactions.

The safety of concomitant use of ZYCLARA Cream and any other imiquimod products has not been established and should be avoided since they contain the same active ingredient (imiquimod) and may increase the risk for and severity of systemic reactions.

Immune Cell Activation in Autoimmune Disease

ZYCLARA Cream should be used with caution in patients with pre-existing autoimmune conditions because imiquimod activates immune cells.

ADVERSE REACTIONS

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Clinical Trials Experience: External Genital Warts

In two double-blind, placebo-controlled studies 602 subjects applied up to one packet of ZYCLARA Cream or vehicle daily for up to 8 weeks.

The most frequently reported adverse reactions were application site reactions and local skin reactions. Selected adverse reactions are listed in Table 1.

Table 1: Selected Adverse Reactions Occurring in ≥2% of ZYCLARA Treated Subjects and at a Greater Frequency than with Vehicle in the Combined Trials (EGW)

Preferred Term	ZYCLARA Cream 3.75% (N=400)	Vehicle Cream (N=202)
Application site pain	28 (7%)	1 (<1%)
Application site irritation	24 (6%)	2 (1%)
Application site pruritus	11 (3%)	2 (1%)
Vaginitis bacterial*	6 (3%)	2 (2%)
Headache	6 (2%)	1 (<1%)

*Percentage based on female population of 6/216 for ZYCLARA Cream 3.75% and 2/106 for vehicle cream

Local skin reactions were recorded as adverse reactions only if they extended beyond the treatment area, if they required any medical intervention, or they resulted in patient discontinuation from the study. The incidence and severity of selected local skin reactions are shown in Table 2.

Table 2: Selected Local Skin Reactions in the Treatment Area Assessed by the Investigator (EGW)

All grades*, (%)	Severe, (%)	ZYCLARA Cream 3.75% (N=400)	Vehicle Cream (N=202)
Erythema*		70%	27%
	Severe erythema	9%	<1%
Edema*		41%	8%
	Severe edema	2%	0%
Erosion/ulceration*		36%	4%
	Severe erosion/ulceration	11%	<1%
Exudate*		34%	2%
	Severe exudate	2%	0%

*Mild, Moderate, or Severe

The frequency and severity of local skin reactions were similar in both genders, with the following exceptions: a) flaking/scaling occurred in 40% of men and in 26% of women and b) scabbing/crusting occurred in 34% of men and in 18% of women.

In the clinical trials, 32% (126/400) of subjects who used ZYCLARA Cream and 2% (4/202) of subjects who used vehicle cream discontinued treatment temporarily (required rest periods) due to adverse local skin reactions, and 1% (3/400) of subjects who used ZYCLARA Cream discontinued treatment permanently due to local skin/application site reactions.

Other adverse reactions reported in subjects treated with ZYCLARA Cream include: rash, back pain, application site rash, application site cellulitis, application site excoriation, application site bleeding, scrotal pain, scrotal erythema, scrotal ulcer, scrotal edema, sinusitis, nausea, pyrexia, and influenza-like symptoms.

Postmarketing Experience

The following adverse reactions have been identified during post-approval use of imiquimod. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Application Site Disorders: tingling at the application site.

Body as a Whole: angioedema.

Cardiovascular: capillary leak syndrome, cardiac failure, cardiomyopathy, pulmonary edema, arrhythmias (tachycardia, supraventricular tachycardia, atrial fibrillation, palpitations), chest pain, ischemia, myocardial infarction, syncope.

Endocrine: thyroiditis.

Gastro-Intestinal System Disorders: abdominal pain.

Hematological: decreases in red cell, white cell and platelet counts (including idiopathic thrombocytopenic purpura), lymphoma.

Hepatic: abnormal liver function.

Infections and Infestations: herpes simplex.

Musculo-Skeletal System Disorders: arthralgia.

Neuropsychiatric: agitation, cerebrovascular accident, convulsions (including febrile convulsions), depression, insomnia, multiple sclerosis aggravation, paresis, suicide.

Respiratory: dyspnea.

Urinary System Disorders: proteinuria, urinary retention, dysuria.

Skin and Appendages: exfoliative dermatitis, erythema multiforme, hyperpigmentation, hypertrophic scar, hypopigmentation.

Vascular: Henoch-Schonlein purpura syndrome.

USE IN SPECIFIC POPULATIONS

Pregnancy Pregnancy Category C:

There are no adequate and well-controlled studies in pregnant women. ZYCLARA Cream should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

The animal multiples of human exposure calculations were based on daily dose comparisons for the reproductive toxicology studies described in this label. The animal multiples of human exposure were based on weekly dose comparisons for the carcinogenicity studies described in this label. For the animal multiple of human exposure ratios presented in this label, the Maximum Recommended Human Dose (MRHD) was set at 2 packets (500 mg cream) per treatment of actinic keratosis with ZYCLARA Cream (imiquimod 3.75%, 18.75 mg imiquimod) for BSA comparison. The maximum human AUC value obtained in the treatment of external genital and perianal warts was higher than that obtained in the treatment of actinic keratosis and was used in the calculation of animal multiples of MRHD that were based on AUC comparison.

Systemic embryofetal development studies were conducted in rats and rabbits. Oral doses of 1, 5 and 20 mg/kg/day imiquimod were administered during the period of organogenesis (gestational days 6 – 15) to pregnant female rats. In the presence of maternal toxicity, fetal effects noted at 20 mg/kg/day (163X MRHD based on AUC comparisons) included increased resorptions, decreased fetal body weight; delays in skeletal ossification, bent limb bones, and two fetuses in one litter (2 of 1567 fetuses) demonstrated exencephaly, protruding tongues and low-set ears. No treatment related effects on embryofetal toxicity or teratogenicity were noted at 5 mg/kg/day (28X MRHD based on AUC comparisons).

Intravenous doses of 0.5, 1 and 2 mg/kg/day imiquimod were administered during the period of organogenesis (gestational days 6 – 18) to pregnant female rabbits. No treatment related effects on embryofetal toxicity or teratogenicity were noted at 2 mg/kg/day (2.1X MRHD based on BSA comparisons; the highest dose evaluated in this study, or 1 mg/kg/day (115X MRHD based on AUC comparisons).

A combined fertility and peri- and post-natal development study was conducted in rats. Oral doses of 1, 1.5, 3 and 6 mg/kg/day imiquimod were administered to male rats from 70 days prior to mating through the mating period and to female rats from 14 days prior to mating through parturition and lactation. No effects on growth, fertility, reproduction or post-natal development were noted at doses up to 6 mg/kg/day (25X MRHD based on AUC comparisons), the highest dose evaluated in this study. In the absence of maternal toxicity, bent limb bones were noted in the F1 fetuses at a dose of 6 mg/kg/day (25X MRHD based on AUC comparisons). This fetal effect was also noted in the oral rat embryofetal development study conducted with imiquimod. No treatment related effects on teratogenicity were noted at 3 mg/kg/day (12X MRHD based on AUC comparisons).

Nursing Mothers

It is not known whether imiquimod is excreted in human milk following use of ZYCLARA Cream. Because many drugs are excreted in human milk, caution should be exercised when ZYCLARA Cream is administered to nursing women.

Pediatric Use

Safety and efficacy in patients with external genital/perianal warts below the age of 12 years have not been established.

Geriatric Use

Clinical studies of ZYCLARA Cream for EGW did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Of the 400 subjects treated with ZYCLARA Cream in the EGW clinical studies, 5 subjects (1%) were 65 years or older.

OVERDOSAGE

Topical overdosing of ZYCLARA Cream could result in an increased incidence of severe local skin reactions and may increase the risk for systemic reactions.

Hypotension was reported in a clinical trial following multiple oral imiquimod doses of >200 mg (equivalent to ingestion of the imiquimod content of more than 21 packets of ZYCLARA). The hypotension resolved following oral or intravenous fluid administration.

Rx Only

GRACEWAY® PHARMACEUTICALS

Manufactured by
3M Health Care Limited
Loughborough LE11 1EP England
Distributed by
Graceway Pharmaceuticals, LLC
Bristol, TN 37620

Issued: March 20
ZYC0911

5400021 Orig

Metaphor, Inc
119 Cherry Hill Road
Parsippany, NJ 07054
973-334-1009

INSERTION ORDER

To:	Alison McCauley	Date:	4/1/11
Fax No.:	646-638-6117	Insertion Order No.:	GRW11049
Tel No.:	646-638-6098	PO#:	ZYC-390
From:	Stefanie Hecht 508-645-9022, 508-645-9021 Fax		
For Insertion In:	CLINICAL ADVISOR		

CLIENT:	Graceway Pharmaceuticals
PRODUCT:	Zyclara
DATE OF ISSUE:	May
AD UNIT:	Page 4CB + Page BW
AD NO.:	ZYC1110186
HEADLINE:	"Effectively Clears Genital Warts"
POSITION:	Far forward
TIME RATE - SPACE:	12x Continuity Rate
COLOR:	1x
NET COST:	$8,653.00
MATERIAL FROM:	New Materials
SPECIAL INSTRUCTIONS:	If materials do not arrive please contact Kathy Heffernan @ 973-334-1009 or kheff@metaphorinc.com

Provisional: ✓
Calculation: ✓
Gross: 10,180
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Invoice No:	44923
Date:	05/26/11
Your Order Ref :	GRW11049
Account No :	540024

Description			Value
Your Client:	**Graceway Pharmaceuticals**		
Publication:	**Clinical Advisor**		
			10,180.00
Cover Date :	01-May-2011		
Your Contact:	Heffernan Kathleen		
Our Salesperson:	Alison McCauley		
Our Booking Ref:	0000099172		
Product:	Zyclara		
Frequency Rate:	12		
Page Number/s:	85,86		
		Agency Disc @ 15%	1,527.00
		Net after Agency Disc	8,653.00
		Net Value	8,653.00

REMITTANCE RECORD

Customer :	METAPHOR INC.	**Payment Terms**	Net 30 Days
Account No :	540024	**Due Date**	**06/25/11**
Invoice No :	44923	**Total Due** USD	8,653.00

Amount Enclosed $

Cheque Number

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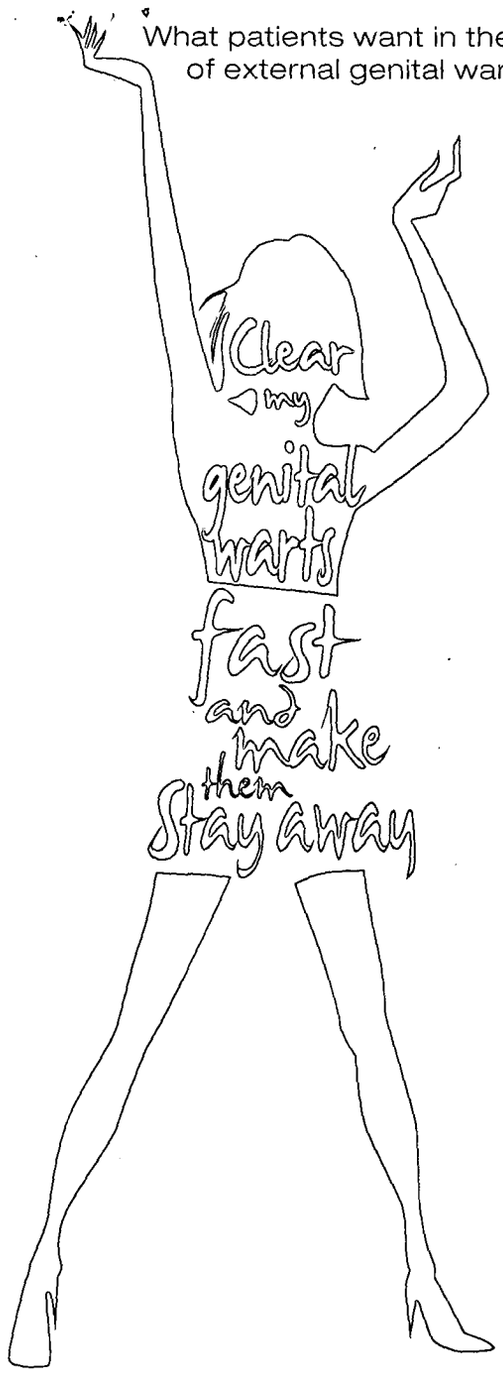
What patients want in the treatment of external genital warts (EGW)...



Effectively clears genital warts and keeps patients clear

Short treatment, daily dosing

- Applied once daily for up to 8 weeks

Significant clearance in females

- 37% complete clearance, 48% partial clearance
  - Partial clearance defined as ≥75% reduction in EGW count from baseline

Patients who clear with Zyclara can expect to remain clear

- Only 15% of patients had a recurrence at 12 weeks posttreatment[1]

Tough on warts, easy on patients

- Low incidence of treatment-related adverse events at the application site: itching (3%), irritation (6%), or pain (7%)[1]
- Local skin reactions, most of which were mild to moderate, included severe erythema (9%) and severe erosion/ulceration (11%)[1]

Zyclara®
(imiquimod) Cream
3.75%

Zyclara Cream is indicated for the treatment of external genital and perianal warts/condyloma acuminata in patients 12 years or older.

In clinical studies, the most frequently reported adverse reactions were local skin and application site reactions. These reactions included erythema, edema, erosion or ulceration, and exudate at the genital wart site. Most local skin reactions were rated as mild to moderate. Intense local inflammatory reactions and/or flu-like systemic signs and symptoms can occur. Dosing interruptions may be required.

Avoid concomitant use of Zyclara Cream and any other imiquimod cream because of increased risk for adverse reactions.

Zyclara Cream is not recommended for the treatment of urethral, intra-vaginal, cervical, rectal, or intra-anal human papilloma viral disease as it has not been studied.

The effect of Zyclara Cream on the transmission of genital warts is unknown. Zyclara Cream may weaken condoms and diaphragms. Sexual contact should be avoided while the cream is on the skin.

Please see Brief Summary of Prescribing Information on adjacent page.

Reference: 1. Data on file. Graceway Pharmaceuticals, LLC.

Zyclara® [zi-clar-a]
(imiquimod) Cream 3.75%

BRIEF SUMMARY OF PRESCRIBING INFORMATION

SEE PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

INDICATIONS AND USAGE

External Genital Warts

ZYCLARA Cream is indicated for the treatment of external genital and perianal warts (EGW)/condyloma acuminata in patients 12 years or older.

Limitations of Use

Treatment with ZYCLARA has not been studied for prevention or transmission of HPV.

Unevaluated Populations

The safety and efficacy of ZYCLARA Cream have not been established in the treatment of:
- urethral, intra-vaginal, cervical, rectal or intra-anal human papilloma viral disease.
- actinic keratosis when treated with more than one 2-cycle treatment course in the same area.
- patients with xeroderma pigmentosum.
- superficial basal cell carcinoma.
- immunosuppressed patients.

CONTRAINDICATIONS None.

WARNINGS AND PRECAUTIONS

Local Skin Reactions

Intense local skin reactions including skin weeping or erosion can occur after a few applications of ZYCLARA Cream and may require an interruption of dosing. ZYCLARA Cream has the potential to exacerbate inflammatory conditions of the skin, including chronic graft versus host disease.

Administration of ZYCLARA Cream is not recommended until the skin is healed from any previous drug or surgical treatment.

Systemic Reactions

Flu-like signs and symptoms may accompany, or even precede, local skin reactions and may include fatigue, nausea, fever, myalgias, arthralgias, malaise and chills. An interruption of dosing and assessment of the patient should be considered.

Lymphadenopathy occurred in 2% of subjects with actinic keratosis treated with ZYCLARA Cream. This reaction resolved in all subjects by 4 weeks after completion of treatment.

Ultraviolet Light Exposure Risks

Exposure to sunlight (including sunlamps) should be avoided or minimized during use of ZYCLARA Cream. Patients should be warned to use protective clothing (e.g., a hat) when using ZYCLARA Cream. Patients with sunburn should be advised not to use ZYCLARA Cream until fully recovered. Patients who may have considerable sun exposure, e.g. due to their occupation, and those patients with inherent sensitivity to sunlight should exercise caution when using ZYCLARA Cream.

In an animal photo-carcinogenicity study, imiquimod cream shortened the time to skin tumor formation. The enhancement of ultraviolet carcinogenicity is not necessarily dependent on phototoxic mechanisms. Therefore, patients should minimize or avoid natural or artificial sunlight exposure.

Increased Risk of Adverse Reactions with Concomitant Imiquimod Use

Concomitant use of ZYCLARA and any other imiquimod products, in the same treatment area, should be avoided since they contain the same active ingredient (imiquimod) and may increase the risk for and severity of local skin reactions.

The safety of concomitant use of ZYCLARA Cream and any other imiquimod products has not been established and should be avoided since they contain the same active ingredient (imiquimod) and may increase the risk for and severity of systemic reactions.

Immune Cell Activation in Autoimmune Disease

ZYCLARA Cream should be used with caution in patients with pre-existing autoimmune conditions because imiquimod activates immune cells.

ADVERSE REACTIONS

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

***Clinical Trials Experience:* External Genital Warts**

In two double-blind, placebo-controlled studies 602 subjects applied up to one packet of ZYCLARA Cream or vehicle daily for up to 8 weeks.

The most frequently reported adverse reactions were application site reactions and local skin reactions. Selected adverse reactions are listed in Table 1.

Table 1: Selected Adverse Reactions Occurring in ≥2% of ZYCLARA Treated Subjects and at a Greater Frequency than with Vehicle in the Combined Trials (EGW)

Preferred Term	ZYCLARA Cream 3.75% (N=400)	Vehicle Cream (N=202)
Application site pain	28 (7%)	1 (<1%)
Application site irritation	24 (6%)	2 (1%)
Application site pruritus	11 (3%)	2 (1%)
Vaginitis bacterial*	6 (3%)	2 (2%)
Headache	6 (2%)	1 (<1%)

*Percentage based on female population of 6/216 for ZYCLARA Cream 3.75% and 2/106 for vehicle cream

Local skin reactions were recorded as adverse reactions only if they extended beyond the treatment area, if they required any medical intervention, or they resulted in patient discontinuation from the study. The incidence and severity of selected local skin reactions are shown in Table 2.

Table 2: Selected Local Skin Reactions in the Treatment Area Assessed by the Investigator (EGW)

All grades*, (%)	Severe, (%)	ZYCLARA Cream 3.75% (N=400)	Vehicle Cream (N=202)
Erythema*		70%	27%
	Severe erythema	9%	<1%
Edema*		41%	8%
	Severe edema	2%	0%
Erosion/ulceration*		36%	4%
	Severe erosion/ulceration	11%	<1%
Exudate*		34%	2%
	Severe exudate	2%	0%

*Mild, Moderate, or Severe

The frequency and severity of local skin reactions were similar in both genders, with the following exceptions: a) flaking/scaling occurred in 40% of men and in 26% of women and b) scabbing/crusting occurred in 34% of men and in 18% of women.

In the clinical trials, 32% (126/400) of subjects who used ZYCLARA Cream and 2% (4/202) of subjects who used vehicle cream discontinued treatment temporarily (required rest periods) due to adverse local skin reactions, and 1% (3/400) of subjects who used ZYCLARA Cream discontinued treatment permanently due to local skin/application site reactions.

Other adverse reactions reported in subjects treated with ZYCLARA Cream include: rash, back pain, application site rash, application site cellulitis, application site excoriation, application site bleeding, scrotal pain, scrotal erythema, scrotal ulcer, scrotal edema, sinusitis, nausea, pyrexia, and influenza-like symptoms.

Postmarketing Experience

The following adverse reactions have been identified during post-approval use of imiquimod. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Application Site Disorders: tingling at the application site.

Body as a Whole: angioedema.

Cardiovascular: capillary leak syndrome, cardiac failure, cardiomyopathy, pulmonary edema, arrhythmias (tachycardia, supraventricular tachycardia, atrial fibrillation, palpitations), chest pain, ischemia, myocardial infarction, syncope.

Endocrine: thyroiditis.

Gastro-Intestinal System Disorders: abdominal pain.

Hematological: decreases in red cell, white cell and platelet counts (including idiopathic thrombocytopenic purpura), lymphoma.

Hepatic: abnormal liver function.

Infections and Infestations: herpes simplex.

Musculo-Skeletal System Disorders: arthralgia.

Neuropsychiatric: agitation, cerebrovascular accident, convulsions (including febrile convulsions), depression, insomnia, multiple sclerosis aggravation, paresis, suicide.

Respiratory: dyspnea.

Urinary System Disorders: proteinuria, urinary retention, dysuria.

Skin and Appendages: exfoliative dermatitis, erythema multiforme, hyperpigmentation, hypertrophic scar, hypopigmentation.

Vascular: Henoch-Schonlein purpura syndrome.

USE IN SPECIFIC POPULATIONS

Pregnancy Pregnancy Category C:

There are no adequate and well-controlled studies in pregnant women. ZYCLARA Cream should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

The animal multiples of human exposure calculations were based on daily dose comparisons for the reproductive toxicology studies described in this label. The animal multiples of human exposure were based on weekly dose comparisons for the carcinogenicity studies described in this label. For the animal multiple of human exposure ratios presented in this label, the Maximum Recommended Human Dose (MRHD) was set at 2 packets (500 mg cream) per treatment of actinic keratosis with ZYCLARA Cream (imiquimod 3.75%, 18.75 mg imiquimod) for BSA comparison. The maximum human AUC value obtained in the treatment of external genital and perianal warts was higher than that obtained in the treatment of actinic keratosis and was used in the calculation of animal multiples of MRHD that were based on AUC comparison.

Systemic embryofetal development studies were conducted in rats and rabbits. Oral doses of 1, 5 and 20 mg/kg/day imiquimod were administered during the period of organogenesis (gestational days 6 – 15) to pregnant female rats. In the presence of maternal toxicity, fetal effects noted at 20 mg/kg/day (163X MRHD based on AUC comparisons) included increased resorptions, decreased fetal body weights, delays in skeletal ossification, bent limb bones, and two fetuses in one litter (2 of 1567 fetuses) demonstrated exencephaly, protruding tongues and low-set ears. No treatment related effects on embryofetal toxicity or teratogenicity were noted at 5 mg/kg/day (28X MRHD based on AUC comparisons).

Intravenous doses of 0.5, 1 and 2 mg/kg/day imiquimod were administered during the period of organogenesis (gestational days 6 – 18) to pregnant female rabbits. No treatment related effects on embryofetal toxicity or teratogenicity were noted at 2 mg/kg/day (2.1X MRHD based on BSA comparisons), the highest dose evaluated in this study, or 1 mg/kg/day (115X MRHD based on AUC comparisons).

A combined fertility and peri- and post-natal development study was conducted in rats. Oral doses of 1, 1.5, 3 and 6 mg/kg/day imiquimod were administered to male rats from 70 days prior to mating through the mating period and to female rats from 14 days prior to mating through parturition and lactation. No effects on growth, fertility, reproduction or post-natal development were noted at doses up to 6 mg/kg/day (25X MRHD based on AUC comparisons), the highest dose evaluated in this study. In the absence of maternal toxicity, bent limb bones were noted in the F1 fetuses at a dose of 6 mg/kg/day (25X MRHD based on AUC comparisons). This fetal effect was also noted in the oral rat embryofetal development study conducted with imiquimod. No treatment related effects on teratogenicity were noted at 3 mg/kg/day (12X MRHD based on AUC comparisons).

Nursing Mothers

It is not known whether imiquimod is excreted in human milk following use of ZYCLARA Cream. Because many drugs are excreted in human milk, caution should be exercised when ZYCLARA Cream is administered to nursing women.

Pediatric Use

Safety and efficacy in patients with external genital/perianal warts below the age of 12 years have not been established.

Geriatric Use

Clinical studies of ZYCLARA Cream for EGW did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Of the 400 subjects treated with ZYCLARA Cream in the EGW clinical studies, 5 subjects (1%) were 65 years or older.

OVERDOSAGE

Topical overdosing of ZYCLARA Cream could result in an increased incidence of severe local skin reactions and may increase the risk for systemic reactions.

Hypotension was reported in a clinical trial following multiple oral imiquimod doses of >200 mg (equivalent to ingestion of the imiquimod content of more than 21 packets of ZYCLARA). The hypotension resolved following oral or intravenous fluid administration.

Rx Only

GRACEWAY® PHARMACEUTICALS

Manufactured by
3M Health Care Limited
Loughborough LE11 1EP England
Distributed by
Graceway Pharmaceuticals, LLC
Bristol, TN 37620

Issued: March 2011
ZYC031137

540024

Metaphor, Inc
119 Cherry Hill Road
Parsippany, NJ 07054
973-334-1009

CMS

INSERTION ORDER

To:	Dominic Barone	Date: 4/1/11	
Fax No.:	646-638-6120	Insertion Order No.: GRW11056	
Tel No.:	646-638-6097	PO#: ZYC-390	
From:	Stefanie Hecht 508-645-9022, 508-645-9021 Fax		
For Insertion In:	JAAPA		

PO# ZYC-390

CLIENT:	Graceway Pharmaceuticals
PRODUCT:	Zyclara
DATE OF ISSUE:	May
AD UNIT:	Page 4CB + Page BW
AD NO.:	ZYC1110188
HEADLINE:	"Thwarted"
POSITION:	Far forward
TIME RATE - SPACE:	48x
COLOR:	1x
NET COST:	$8,321.50
MATERIAL FROM:	New Materials
SPECIAL INSTRUCTIONS:	If materials do not arrive please contact Kathy Heffernan at 973-334-1009 or kheff@metaphorinc.com

Provisional ✓
Calculation ✓
Gross: 9,790
Net: 8,321.50

NAME DATE

Please send Invoices to: Kathleen Heffernan, Production Supervisor, Metaphor, Inc., 119 Cherry Hill Road, Parsippany, NJ 07054. 973-334-1009

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New York, NY 10001
Tel (646) 638-6000

COPY INVOICE

HEFFERNAN KATHLEEN
METAPHOR INC.
119 CHERRY HILL ROAD
PARSIPPANY, NJ, 07054

Invoice No:	44842
Date:	05/24/11
Your Order Ref :	GRW11056
Account No :	540024

Description			Value
Your Client:	**Graceway Pharmaceuticals**		
Publication:	**JAAPA**		
			9,790.00
Cover Date :	01-May-2011		
Your Contact:	Heffernan Kathleen		
Our Salesperson:	Dominic Barone		
Our Booking Ref:	0000099091		
Product:	Zyclara		
Frequency Rate:	48		
Page Number/s:	7,8		
		Agency Disc @ 15%	1,468.50
PO #ZYC-390			
		Net after Agency Disc	8,321.50
		Net Value	8,321.50

REMITTANCE RECORD

Customer :	METAPHOR INC.	**Payment Terms**	Net 30 Days
Account No :	540024	**Due Date**	**06/23/11**
Invoice No :	44842	**Total Due** USD	8,321.50

Amount Enclosed $

Cheque Number

Please make all cheques payable to **Haymarket Media, Inc. PO BOX 512368, Philadelphia, PA 19175-2368** and remit to this address with this bottom portion of the invoice. Thank You.

GENITAL WARTS

THWARTED!

Short treatment, daily dosing

- Applied once daily for up to 8 weeks[1]

Significant clearance of external genital warts[1]

In females–

- 37% complete clearance; 48% partial clearance

In males–

- 19% complete clearance; 27% partial clearance
  – Partial clearance defined as ≥75% reduction in EGW count from baseline

Many patients who cleared with Zyclara remained clear[1]

- Only 15% of patients had a recurrence at 12 weeks posttreatment

Tough on warts, easy on patients

- Low incidence of treatment-related adverse events at the application site: itching (3%), irritation (6%), or pain (7%)[1]
- Local skin reactions, most of which were mild to moderate, included severe erythema (9%) and severe erosion/ulceration (11%)[1]

Zyclara®
(imiquimod) Cream
3.75%

Zyclara Cream is indicated for the treatment of external genital and perianal warts/condyloma acuminata in patients 12 years or older.

In clinical studies, the most frequently reported adverse reactions were local skin and application site reactions. These reactions included erythema, edema, erosion or ulceration, and exudate at the genital wart site. Most local skin reactions were rated as mild to moderate. Intense local inflammatory reactions and/or flu-like systemic signs and symptoms can occur. Dosing interruptions may be required.

Avoid concomitant use of Zyclara Cream and any other imiquimod cream because of increased risk for adverse reactions.

Zyclara Cream is not recommended for the treatment of urethral, intra-vaginal, cervical, rectal, or intra-anal human papilloma viral disease as it has not been studied.

The effect of Zyclara Cream on the transmission of genital warts is unknown. Zyclara Cream may weaken condoms and diaphragms. Sexual contact should be avoided while the cream is on the skin.

Please see Brief Summary of Prescribing Information on adjacent page.

Reference: 1. Data on file, Graceway Pharmaceuticals, LLC.

Zyclara® [zi-clar-a]
(imiquimod) Cream 3.75%

BRIEF SUMMARY OF PRESCRIBING INFORMATION

SEE PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

INDICATIONS AND USAGE

External Genital Warts

ZYCLARA Cream is indicated for the treatment of external genital and perianal warts (EGW)/condyloma acuminata in patients 12 years or older.

Limitations of Use

Treatment with ZYCLARA has not been studied for prevention or transmission of HPV.

Unevaluated Populations

The safety and efficacy of ZYCLARA Cream have not been established in the treatment of:
- urethral, intra-vaginal, cervical, rectal or intra-anal human papilloma viral disease.
- actinic keratosis when treated with more than one 2-cycle treatment course in the same area.
- patients with xeroderma pigmentosum.
- superficial basal cell carcinoma.
- immunosuppressed patients.

CONTRAINDICATIONS None.

WARNINGS AND PRECAUTIONS

Local Skin Reactions

Intense local skin reactions including skin weeping or erosion can occur after a few applications of ZYCLARA Cream and may require an interruption of dosing. ZYCLARA Cream has the potential to exacerbate inflammatory conditions of the skin, including chronic graft versus host disease.

Administration of ZYCLARA Cream is not recommended until the skin is healed from any previous drug or surgical treatment.

Systemic Reactions

Flu-like signs and symptoms may accompany, or even precede, local skin reactions and may include fatigue, nausea, fever, myalgias, arthralgias, malaise and chills. An interruption of dosing and assessment of the patient should be considered.

Lymphadenopathy occurred in 2% of subjects with actinic keratosis treated with ZYCLARA Cream. This reaction resolved in all subjects by 4 weeks after completion of treatment.

Ultraviolet Light Exposure Risks

Exposure to sunlight (including sunlamps) should be avoided or minimized during use of ZYCLARA Cream. Patients should be warned to use protective clothing (e.g., a hat) when using ZYCLARA Cream. Patients with sunburn should be advised not to use ZYCLARA Cream until fully recovered. Patients who may have considerable sun exposure, e.g. due to their occupation, and those patients with inherent sensitivity to sunlight should exercise caution when using ZYCLARA Cream.

In an animal photo-carcinogenicity study, imiquimod cream shortened the time to skin tumor formation. The enhancement of ultraviolet carcinogenicity is not necessarily dependent on phototoxic mechanisms. Therefore, patients should minimize or avoid natural or artificial sunlight exposure.

Increased Risk of Adverse Reactions with Concomitant Imiquimod Use

Concomitant use of ZYCLARA and any other imiquimod products, in the same treatment area, should be avoided since they contain the same active ingredient (imiquimod) and may increase the risk for and severity of local skin reactions.

The safety of concomitant use of ZYCLARA Cream and any other imiquimod products has not been established and should be avoided since they contain the same active ingredient (imiquimod) and may increase the risk for and severity of systemic reactions.

Immune Cell Activation in Autoimmune Disease

ZYCLARA Cream should be used with caution in patients with pre-existing autoimmune conditions because imiquimod activates immune cells.

ADVERSE REACTIONS

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Clinical Trials Experience: External Genital Warts

In two double-blind, placebo-controlled studies 602 subjects applied up to one packet of ZYCLARA Cream or vehicle daily for up to 8 weeks.

The most frequently reported adverse reactions were application site reactions and local skin reactions. Selected adverse reactions are listed in Table 1.

Table 1: Selected Adverse Reactions Occurring in ≥2% of ZYCLARA Treated Subjects and at a Greater Frequency than with Vehicle in the Combined Trials (EGW)

Preferred Term	ZYCLARA Cream 3.75% (N=400)	Vehicle Cream (N=202)
Application site pain	28 (7%)	1 (<1%)
Application site irritation	24 (6%)	2 (1%)
Application site pruritus	11 (3%)	2 (1%)
Vaginitis bacterial*	6 (3%)	2 (2%)
Headache	6 (2%)	1 (<1%)

*Percentage based on female population of 6/216 for ZYCLARA Cream 3.75% and 2/106 for vehicle cream

Local skin reactions were recorded as adverse reactions only if they extended beyond the treatment area, if they required any medical intervention, or they resulted in patient discontinuation from the study. The incidence and severity of selected local skin reactions are shown in Table 2.

Table 2: Selected Local Skin Reactions in the Treatment Area Assessed by the Investigator (EGW)

All grades*, (%) / Severe, (%)	ZYCLARA Cream 3.75% (N=400)	Vehicle Cream (N=202)
Erythema*	70%	27%
Severe erythema	9%	<1%
Edema*	41%	8%
Severe edema	2%	0%
Erosion/ulceration*	36%	4%
Severe erosion/ulceration	11%	<1%
Exudate*	34%	2%
Severe exudate	2%	0%

*Mild, Moderate, or Severe

The frequency and severity of local skin reactions were similar in both genders, with the following exceptions: a) flaking/scaling occurred in 40% of men and in 26% of women and b) scabbing/crusting occurred in 34% of men and in 18% of women.

In the clinical trials, 32% (126/400) of subjects who used ZYCLARA Cream and 2% (4/202) of subjects who used vehicle cream discontinued treatment temporarily (required rest periods) due to adverse local skin reactions, and 1% (3/400) of subjects who used ZYCLARA Cream discontinued treatment permanently due to local skin/application site reactions.

Other adverse reactions reported in subjects treated with ZYCLARA Cream include: rash, back pain, application site rash, application site cellulitis, application site excoriation, application site bleeding, scrotal pain, scrotal erythema, scrotal ulcer, scrotal edema, sinusitis, nausea, pyrexia, and influenza-like symptoms.

Postmarketing Experience

The following adverse reactions have been identified during post-approval use of imiquimod. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Application Site Disorders: tingling at the application site.

Body as a Whole: angioedema.

Cardiovascular: capillary leak syndrome, cardiac failure, cardiomyopathy, pulmonary edema, arrhythmias (tachycardia, supraventricular tachycardia, atrial fibrillation, palpitations), chest pain, ischemia, myocardial infarction, syncope.

Endocrine: thyroiditis.

Gastro-Intestinal System Disorders: abdominal pain.

Hematological: decreases in red cell, white cell and platelet counts (including idiopathic thrombocytopenic purpura), lymphoma.

Hepatic: abnormal liver function.

Infections and Infestations: herpes simplex.

Musculo-Skeletal System Disorders: arthralgia.

Neuropsychiatric: agitation, cerebrovascular accident, convulsions (including febrile convulsions), depression, insomnia, multiple sclerosis aggravation, paresis, suicide.

Respiratory: dyspnea.

Urinary System Disorders: proteinuria, urinary retention, dysuria.

Skin and Appendages: exfoliative dermatitis, erythema multiforme, hyperpigmentation, hypertrophic scar, hypopigmentation.

Vascular: Henoch-Schonlein purpura syndrome.

USE IN SPECIFIC POPULATIONS

Pregnancy Pregnancy Category C:

There are no adequate and well-controlled studies in pregnant women. ZYCLARA Cream should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

The animal multiples of human exposure calculations were based on daily dose comparisons for the reproductive toxicology studies described in this label. The animal multiples of human exposure were based on weekly dose comparisons for the carcinogenicity studies described in this label. For the animal multiple of human exposure ratios presented in this label, the Maximum Recommended Human Dose (MRHD) was set at 2 packets (500 mg cream) per treatment of actinic keratosis with ZYCLARA Cream (imiquimod 3.75%, 18.75 mg imiquimod) for BSA comparison. The maximum human AUC value obtained in the treatment of external genital and perianal warts was higher than that obtained in the treatment of actinic keratosis and was used in the calculation of animal multiples of MRHD that were based on AUC comparison.

Systemic embryofetal development studies were conducted in rats and rabbits. Oral doses of 1, 5 and 20 mg/kg/day imiquimod were administered during the period of organogenesis (gestational days 6 – 15) to pregnant female rats. In the presence of maternal toxicity, fetal effects noted at 20 mg/kg/day (163X MRHD based on AUC comparisons) included increased resorptions, decreased fetal body weights, delays in skeletal ossification, bent limb bones, and two fetuses in one litter (2 of 1567 fetuses) demonstrated exencephaly, protruding tongues and low-set ears. No treatment related effects on embryofetal toxicity or teratogenicity were noted at 5 mg/kg/day (28X MRHD based on AUC comparisons).

Intravenous doses of 0.5, 1 and 2 mg/kg/day imiquimod were administered during the period of organogenesis (gestational days 6 – 18) to pregnant female rabbits. No treatment related effects on embryofetal toxicity or teratogenicity were noted at 2 mg/kg/day (2.1X MRHD based on BSA comparisons), the highest dose evaluated in this study, or 1 mg/kg/day (115X MRHD based on AUC comparisons).

A combined fertility and peri- and post-natal development study was conducted in rats. Oral doses of 1, 1.5, 3 and 6 mg/kg/day imiquimod were administered to male rats from 70 days prior to mating through the mating period and to female rats from 14 days prior to mating through parturition and lactation. No effects on growth, fertility, reproduction or post-natal development were noted at doses up to 6 mg/kg/day (25X MRHD based on AUC comparisons), the highest dose evaluated in this study. In the absence of maternal toxicity, bent limb bones were noted in the F1 fetuses at a dose of 6 mg/kg/day (25X MRHD based on AUC comparisons). This fetal effect was also noted in the oral rat embryofetal development study conducted with imiquimod. No treatment related effects on teratogenicity were noted at 3 mg/kg/day (12X MRHD based on AUC comparisons).

Nursing Mothers

It is not known whether imiquimod is excreted in human milk following use of ZYCLARA Cream. Because many drugs are excreted in human milk, caution should be exercised when ZYCLARA Cream is administered to nursing women.

Pediatric Use

Safety and efficacy in patients with external genital/perianal warts below the age of 12 years have not been established.

Geriatric Use

Clinical studies of ZYCLARA Cream for EGW did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Of the 400 subjects treated with ZYCLARA Cream in the EGW clinical studies, 5 subjects (1%) were 65 years or older.

OVERDOSAGE

Topical overdosing of ZYCLARA Cream could result in an increased incidence of severe local skin reactions and may increase the risk for systemic reactions.

Hypotension was reported in a clinical trial following multiple oral imiquimod doses of >200 mg (equivalent to ingestion of the imiquimod content of more than 21 packets of ZYCLARA). The hypotension resolved following oral or intravenous fluid administration.

Rx Only

GRACEWAY® PHARMACEUTICALS

Manufactured by
3M Health Care Limited
Loughborough LE11 1EP England
Distributed by
Graceway Pharmaceuticals, LLC
Bristol, TN 37620

Issued: March 2011
ZYC031137

CMS

Metaphor, Inc
119 Cherry Hill Road
Parsippany, NJ 07054
973-334-1009

INSERTION ORDER

To: Alison McCauley Date: 2/22/11

Fax No.: 646-638-6117 Insertion Order No.: GRW11035

Tel No.: 646-638-6098 PO#: ZYC-375

From: Stefanie Hecht 508-645-9022, 508-645-9021 Fax

PO#: ZYC-375

For Insertion In: CLINICAL ADVISOR

CLIENT:	Graceway Pharmaceuticals
PRODUCT:	Zyclara
DATE OF ISSUE:	April
AD UNIT:	Page 4CB + Page BW
AD NO.:	ZYC0310102
HEADLINE:	"Significant Lesion Reduction With Long-term Benefits"
POSITION:	Far forward
TIME RATE - SPACE:	12x Continuity Rate
COLOR:	1x
NET COST:	$8,653.00
MATERIAL FROM:	Repeat from March
SPECIAL INSTRUCTIONS:	

Provisional: ✓
Calculation: ✓
Gross: $10,180
Net: 8,653

NAME DATE

Please send invoices to: Kathleen Heffernan, Production Supervisor, Metaphor, Inc., 119 Cherry Hill Road, Parsippany, NJ 07054. 973-334-1009

IF INCLUDED, PRESCRIBING INFORMATION MUST RUN IMMEDIATELY ADJACENT TO AD

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HEFFERNAN KATHLEEN
METAPHOR INC.
119 CHERRY HILL ROAD
PARSIPPANY, NJ, 07054

Invoice No:	44388
Date:	04/28/11
Your Order Ref :	GRW11035
Account No :	540024

Description			Value
Your Client:	**Graceway Pharmaceuticals**		
Publication:	**Clinical Advisor**		
			10,180.00
Cover Date :	01-April-2011		
Your Contact:	Heffernan Kathleen		
Our Salesperson:	Alison McCauley		
Our Booking Ref:	0000098687		
Product:	Zyclara		
Frequency Rate:	12		
Page Number/s:	51,52		
		Agency Disc @ 15%	1,527.00
PO# ZYC-375			
		Net after Agency Disc	8,653.00
		Net Value	8,653.00

REMITTANCE RECORD

Customer :	METAPHOR INC.	**Payment Terms**		Net 30 Days
Account No :	540024	**Due Date**		**05/28/11**
Invoice No :	44388	**Total Due**	USD	8,653.00

Amount Enclosed $

Cheque Number

Please make all cheques payable to **Haymarket Media, Inc. PO BOX 512368, Philadelphia, PA 19175-2368** and remit to this address with this bottom portion of the invoice. Thank You.

For the treatment of actinic keratosis—
Zyclara

Significant lesion reduction with long-term benefits

Once-daily dosing in a simple course

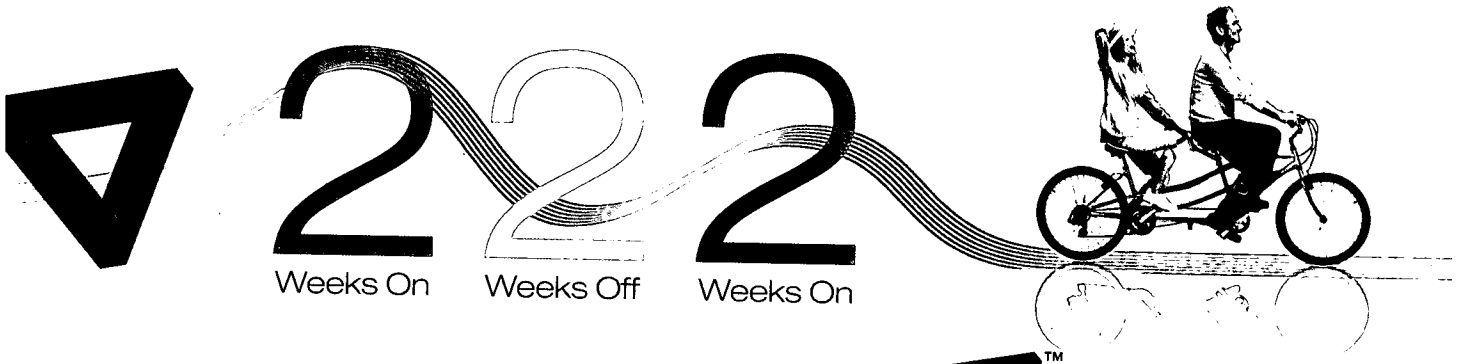
- 2 weeks on / 2 weeks off / 2 weeks on
- 94% compliance rate with the dosing schedule in clinical trials[1]
  - Compliance defined as patients who received 75% or more of prescribed medication

Many patients who cleared with Zyclara remained clear

- 36% of patients had complete clearance[1]
- 59% had partial clearance[1]
  - Partial clearance defined as >75% reduction in the number of lesions at baseline
- 82% reduction in overall lesion count[1]
- 40% of patients with complete clearance remained lesion free at 12 months posttreatment[2]

Treats the lesions you can see—and the ones you can't[1]

- 86% of patients had previously undetected lesions revealed and treated



Zyclara™
(imiquimod) Cream
3.75%

Zyclara Cream is indicated for the topical treatment of clinically typical visible or palpable actinic keratoses (AK) of the full face or balding scalp in immunocompetent adults.

In clinical studies, the most common side effects involved skin reactions in the application area. These reactions included erythema, scabbing or crusting, flaking, scaling or dryness, edema, erosion or ulceration, and weeping or exudate. Most skin reactions were rated as mild to moderate. Intense local inflammatory reactions and/or flu-like systemic signs and symptoms can occur. Dosing interruptions may be required.

Exposure to natural or artificial sunlight (tanning beds or UVA/B treatment) should be avoided or minimized during use of Zyclara Cream.

Please see Brief Summary of Full Prescribing Information on adjacent page.

Visit us at **www.ZyclaraCream.com**

References: 1. Swanson N, Abramovits W, Berman B, et al. Imiquimod 2.5% and 3.75% for the treatment of actinic keratoses: results of 2 placebo-controlled studies of daily application to the face and balding scalp for two 2-week cycles. *J Am Acad Dermatol.* 2010;62(4):582-590. **2.** Swanson N, Hanke CW, Berman B, et al. Twelve month sustained clearance of actinic keratosis of the full face or balding scalp after imiquimod 2.5% and 3.75% applied daily for two 2-week or 3-week cycles. Poster presented at: 68th American Academy of Dermatology Annual Meeting; March 2010; Miami, FL.

GRACEWAY® PHARMACEUTICALS

Zyclara™ [zi-clar-a]
(imiquimod) Cream 3.75%

BRIEF SUMMARY OF PRESCRIBING INFORMATION

SEE PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

INDICATIONS AND USAGE

Actinic Keratosis

ZYCLARA Cream is indicated for the topical treatment of clinically typical visible or palpable actinic keratoses (AK), of the full face or balding scalp in immunocompetent adults.

Unevaluated Populations

Safety and efficacy have not been established for ZYCLARA Cream in the treatment of actinic keratosis, with more than one 2-cycle treatment course in the same area.

The safety and efficacy of ZYCLARA Cream in immunosuppressed patients have not been established.

The safety and efficacy have not been established for ZYCLARA Cream in the treatment of patients with xeroderma pigmentosum.

The safety and efficacy have not been established for ZYCLARA Cream in the treatment of superficial basal cell carcinoma.

The safety and efficacy have not been established for ZYCLARA Cream in the treatment of external genital warts.

ZYCLARA Cream should be used with caution in patients with pre-existing autoimmune conditions.

CONTRAINDICATIONS

None (4)

WARNINGS AND PRECAUTIONS

Local Skin Reactions

Intense local skin reactions including skin weeping or erosion can occur after a few applications of ZYCLARA Cream and may require an interruption of dosing. *[see Dosage and Administration (2) and Adverse Reactions (6)]*. ZYCLARA Cream has the potential to exacerbate inflammatory conditions of the skin, including chronic graft versus host disease.

Administration of ZYCLARA Cream is not recommended until the skin is healed from any previous drug or surgical treatment.

Concomitant use of ZYCLARA and any other imiquimod creams, in the same treatment area, should be avoided since they contain the same active ingredient (imiquimod) and may increase the risk for and severity of local skin reactions.

Systemic Reactions

Flu-like signs and symptoms may accompany, or even precede, local skin reactions and may include fatigue, nausea, fever, myalgias, arthralgias, and chills. An interruption of dosing and an assessment of the patient should be considered. *[see Adverse Reactions (6)]*

Lymphadenopathy occurred in 2% of subjects treated with ZYCLARA Cream *[see Adverse Reactions (6)]*. This reaction resolved in all subjects by 4 weeks after completion of treatment.

The safety of concomitant use of ZYCLARA Cream and any other imiquimod creams has not been established and should be avoided since they contain the same active ingredient (imiquimod) and may increase the risk for and severity of systemic reactions.

Ultraviolet Light Exposure

Exposure to sunlight (including sunlamps) should be avoided or minimized during use of ZYCLARA Cream because of concern for heightened sunburn susceptibility. Patients should be warned to use protective clothing (e.g., a hat) when using ZYCLARA Cream. Patients with sunburn should be advised not to use ZYCLARA Cream until fully recovered. Patients who may have considerable sun exposure, e.g., due to their occupation, and those patients with inherent sensitivity to sunlight should exercise caution when using ZYCLARA Cream.

In an animal photo-carcinogenicity study, imiquimod cream shortened the time to skin tumor formation *[see Nonclinical Toxicology (13.1)]*. The enhancement of ultraviolet carcinogenicity is not necessarily dependent on phototoxic mechanisms. Therefore, patients should minimize or avoid natural or artificial sunlight exposure.

ADVERSE REACTIONS

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Clinical Trials Experience

The data described below reflect exposure to ZYCLARA Cream or placebo in 319 subjects enrolled in two double-blind, vehicle-controlled studies. Subjects applied up to two packets of ZYCLARA Cream or vehicle daily to the skin of the affected area (either entire face or balding scalp) for two 2-week treatment cycles separated by a 2-week no-treatment period.

Table 1: Selected Adverse Reactions Occurring in ≥2% of ZYCLARA-Treated Subjects and at a Greater Frequency Than With Vehicle in the Combined Studies

Preferred Term	ZYCLARA Cream 3.75% (N=160)	Vehicle (N=159)
Headache	10 (6%)	5 (3%)
Application site pruritus	7 (4%)	1 (<1%)
Fatigue	7 (4%)	0 (0%)
Nausea	6 (3%)	2 (1%)
Application site irritation	5 (3%)	0 (0%)
Application site pain	5 (3%)	0 (0%)
Pyrexia	5 (3%)	0 (0%)
Anorexia	4 (3%)	0 (0%)
Dizziness	4 (3%)	0 (0%)
Herpes simplex	4 (3%)	1 (<1%)
Pain	4 (3%)	0 (0%)
Chest pain	3 (2%)	0 (0%)
Diarrhea	3 (2%)	0 (0%)
Lymphadenopathy	3 (2%)	0 (0%)

Table 2: Local Skin Reactions in the Treatment Area in ZYCLARA-Treated Subjects as Assessed by the Investigator

	ZYCLARA Cream 3.75% (n=160)		Vehicle (n=159)	
	All Grades*	Severe	All Grades*	Severe
Erythema	154 (96%)	40 (25%)	124 (78%)	0 (0%)
Scabbing/Crusting	149 (93%)	22 (14%)	72 (45%)	0 (0%)
Flaking/Scaling/Dryness	147 (92%)	13 (8%)	123 (77%)	2 (1%)
Edema	120 (75%)	9 (6%)	31 (19%)	0 (0%)
Erosion/Ulceration	99 (62%)	17 (11%)	14 (9%)	0 (0%)
Weeping/Exudate	81 (51%)	9 (6%)	6 (4%)	0 (0%)

*All Grades: mild, moderate or severe

Local skin reactions may extend beyond treatment area.

Overall, in the clinical trials, 11% (17/160) of subjects on ZYCLARA Cream and 0% on vehicle cream required rest periods due to adverse reactions.

Other adverse reactions observed in subjects treated with ZYCLARA Cream include: application site bleeding, application site swelling, arthralgia, cheilitis, chills, dermatitis, herpes zoster, influenza-like illness, insomnia, lethargy, myalgia, pancytopenia, pruritus, squamous cell carcinoma, and vomiting.

Postmarketing Experience

There are currently no postmarketing adverse reactions reported for ZYCLARA Cream.

The following adverse reactions have been identified during post-approval use of Aldara (imiquimod) Cream, 5%. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Body as a Whole: angioedema.

Cardiovascular: capillary leak syndrome, cardiac failure, cardiomyopathy, pulmonary edema, arrhythmias (tachycardia, supraventricular tachycardia, atrial fibrillation, palpitations), chest pain, ischemia, myocardial infarction, syncope.

Endocrine: thyroiditis.

Gastro-Intestinal System Disorders: abdominal pain.

Hematological: decreases in red cell, white cell and platelet counts (including idiopathic thrombocytopenic purpura), lymphoma.

Hepatic: abnormal liver function.

Infections and Infestations: herpes simplex.

Neuropsychiatric: agitation, cerebrovascular accident, convulsions (including febrile convulsions), depression, insomnia, multiple sclerosis aggravation, paresis, suicide.

Respiratory: dyspnea.

Urinary System Disorders: proteinuria, urinary retention, dysuria.

Skin and Appendages: exfoliative dermatitis, erythema multiforme, hyperpigmentation, hypertrophic scar.

Vascular: Henoch-Schonlein purpura syndrome.

USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Category C:

There are no adequate and well-controlled studies in pregnant women. ZYCLARA Cream should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Note: The animal multiples of human exposure calculations were based on daily dose comparisons for the reproductive toxicology studies described in this label. The animal multiples of human exposure were based on weekly dose comparisons for the carcinogenicity studies described in this label. For the animal multiple of human exposure ratios presented in this label, the Maximum Recommended Human Dose (MRHD) was set at 2 packets (500 mg cream) per treatment of ZYCLARA Cream (imiquimod 3.75%, 18.75 mg imiquimod).

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Hypotension was reported in a clinical trial following multiple oral imiquimod doses of >200 mg (equivalent to the ingestion of imiquimod content of >21 packets of ZYCLARA). This resolved following oral or intravenous fluid administration.

Rx Only

GRACEWAY® PHARMACEUTICALS

Manufactured by
3M Health Care Limited
Loughborough LE11 1EP England

Distributed by
Graceway Pharmaceuticals, LLC
Bristol, TN 37620

Issued: March 2010
ZYC0410135

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Metaphor, Inc
119 Cherry Hill Road
Parsippany, NJ 07054
973-334-1009

CMS

INSERTION ORDER

To: Dominic Barone

Date: 2/22/11

Fax No.: 646-638-6120

Insertion Order No.: GRW11039

Tel No.: 646-638-6097

PO#: ZYC-375

From: Stefanie Hecht 508-645-9022, 508-645-9021 Fax

For Insertion In: JAAPA

CLIENT:	Graceway Pharmaceuticals
PRODUCT:	Zyclara
DATE OF ISSUE:	April
AD UNIT:	Page 4CB + Page BW
AD NO.:	ZYC0910179a
HEADLINE:	"What Will Your Patients Pay for Significant Lesion Reduction"
POSITION:	Far forward
TIME RATE - SPACE:	48x
COLOR:	1x
NET COST:	$8,321.50
MATERIAL FROM:	Repeat from February
SPECIAL INSTRUCTIONS:	

Provisional: ✓
Calculation: ✓
Gross: 9,790
Net: 8,321.50

NAME DATE

Please send invoices to: Kathleen Heffernan, Production Supervisor, Metaphor, Inc., 119 Cherry Hill Road, Parsippany, NJ 07054. 973-334-1009

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HEFFERNAN KATHLEEN
METAPHOR INC.
119 CHERRY HILL ROAD
PARSIPPANY, NJ, 07054

Invoice No:	44291
Date:	04/26/11
Your Order Ref :	GRW11039
Account No :	540024

Description			Value
Your Client:	**Graceway Pharmaceuticals**		
Publication:	**JAAPA**		
			9,790.00
Cover Date :	01-April-2011		
Your Contact:	Heffernan Kathleen		
Our Salesperson:	Dominic Barone		
Our Booking Ref:	0000098590		
Product:	Zyclara		
Frequency Rate:	48		
Page Number/s:	21,22		
		Agency Disc @ 15%	1,468.50
PO #ZYC-375			
		Net after Agency Disc	8,321.50
		Net Value	8,321.50

REMITTANCE RECORD

Customer :	METAPHOR INC.
Account No :	540024
Invoice No :	44291

Payment Terms		Net 30 Days
Due Date		**05/26/11**
Total Due	USD	8,321.50

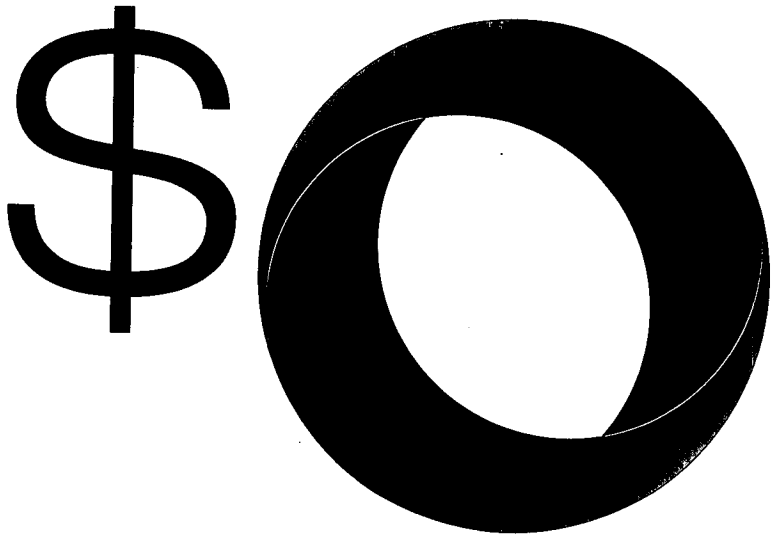
Amount Enclosed $

Cheque Number

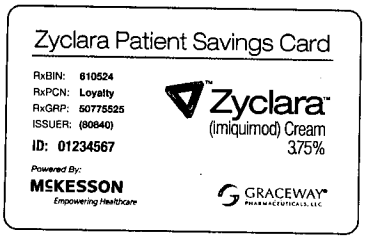
Please make all cheques payable to **Haymarket Media, Inc. PO BOX 512368, Philadelphia, PA 19175-2368** and remit to this address with this bottom portion of the invoice. Thank You.

In the treatment of actinic keratosis

What will your patients pay for significant lesion reduction?



The Zyclara Zero Program



Most card holders pay $0 per prescription

- Maximum benefit of $300 per use
- Limit of 2 uses per card; some restrictions apply*

Zyclara®
(imiquimod) Cream
3.75%

- 36% of patients had complete clearance vs 6% for placebo ($P<.001$)[1]
- 59% had partial clearance vs 23% for placebo ($P<.001$)[1]

Zyclara Cream is indicated for the topical treatment of clinically typical visible or palpable actinic keratoses (AK) of the full face or balding scalp in immunocompetent adults.

In clinical studies, the most common side effects involved skin reactions in the application area. These reactions included erythema, scabbing or crusting, flaking, scaling or dryness, edema, erosion or ulceration, and weeping or exudate. Most skin reactions were rated as mild to moderate. Intense local inflammatory reactions and/or flu-like systemic signs and symptoms can occur. Dosing interruptions may be required.

Exposure to natural or artificial sunlight (tanning beds or UVA/B treatment) should be avoided or minimized during use of Zyclara Cream.

Please see Brief Summary of Full Prescribing Information on adjacent page.

Visit us at **www.ZyclaraCream.com**

*Patient not eligible if any one of the following apply: (1) prescriptions are paid in part or.full by any state or federally funded programs including but not limited to Medicare or Medicaid, Medigap, VA, DOD, or TriCare; (2) patient does not have any prescription drug benefits; (3) patient is a resident of MA; (4) where prohibited by law; (5) patient is under the age of 18. LoyaltyScript® is not an insurance card.

For questions regarding setup, claim transmission, patient eligibility, or other issues, call the ZYCLARA Patient Savings Card Program at 1-877-264-2440 (8:00 AM through 8:00 PM EST, Monday through Friday).

Reference: 1. Swanson N, Abramovits W, Berman B, et al. Imiquimod 2.5% and 3.75% for the treatment of actinic keratoses: results of 2 placebo-controlled studies of daily application to the face and balding scalp for two 2-week cycles. *J Am Acad Dermatol.* 2010;62(4):582-590.

GRACEWAY® PHARMACEUTICALS

Zyclara™ [zi-clar-a]
(imiquimod) Cream 3.75%

BRIEF SUMMARY OF PRESCRIBING INFORMATION

SEE PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

INDICATIONS AND USAGE

Actinic Keratosis

ZYCLARA Cream is indicated for the topical treatment of clinically typical visible or palpable actinic keratoses (AK), of the full face or balding scalp in immunocompetent adults.

Unevaluated Populations

Safety and efficacy have not been established for ZYCLARA Cream in the treatment of actinic keratosis, with more than one 2-cycle treatment course in the same area.

The safety and efficacy of ZYCLARA Cream in immunosuppressed patients have not been established.

The safety and efficacy have not been established for ZYCLARA Cream in the treatment of patients with xeroderma pigmentosum.

The safety and efficacy have not been established for ZYCLARA Cream in the treatment of superficial basal cell carcinoma.

The safety and efficacy have not been established for ZYCLARA Cream in the treatment of external genital warts.

ZYCLARA Cream should be used with caution in patients with pre-existing autoimmune conditions.

CONTRAINDICATIONS

None (4)

WARNINGS AND PRECAUTIONS

Local Skin Reactions

Intense local skin reactions including skin weeping or erosion can occur after a few applications of ZYCLARA Cream and may require an interruption of dosing. *[see Dosage and Administration (2) and Adverse Reactions (6)]*. ZYCLARA Cream has the potential to exacerbate inflammatory conditions of the skin, including chronic graft versus host disease.

Administration of ZYCLARA Cream is not recommended until the skin is healed from any previous drug or surgical treatment.

Concomitant use of ZYCLARA and any other imiquimod creams, in the same treatment area, should be avoided since they contain the same active ingredient (imiquimod) and may increase the risk for and severity of local skin reactions.

Systemic Reactions

Flu-like signs and symptoms may accompany, or even precede, local skin reactions and may include fatigue, nausea, fever, myalgias, arthralgias, and chills. An interruption of dosing and an assessment of the patient should be considered. *[see Adverse Reactions (6)]*

Lymphadenopathy occurred in 2% of subjects treated with ZYCLARA Cream *[see Adverse Reactions (6)]*. This reaction resolved in all subjects by 4 weeks after completion of treatment.

The safety of concomitant use of ZYCLARA Cream and any other imiquimod creams has not been established and should be avoided since they contain the same active ingredient (imiquimod) and may increase the risk for and severity of systemic reactions.

Ultraviolet Light Exposure

Exposure to sunlight (including sunlamps) should be avoided or minimized during use of ZYCLARA Cream because of concern for heightened sunburn susceptibility. Patients should be warned to use protective clothing (e.g., a hat) when using ZYCLARA Cream. Patients with sunburn should be advised not to use ZYCLARA Cream until fully recovered. Patients who may have considerable sun exposure, e.g., due to their occupation, and those patients with inherent sensitivity to sunlight should exercise caution when using ZYCLARA Cream.

In an animal photo-carcinogenicity study, imiquimod cream shortened the time to skin tumor formation *[see Nonclinical Toxicology (13.1)]*. The enhancement of ultraviolet carcinogenicity is not necessarily dependent on phototoxic mechanisms. Therefore, patients should minimize or avoid natural or artificial sunlight exposure.

ADVERSE REACTIONS

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Clinical Trials Experience

The data described below reflect exposure to ZYCLARA Cream or placebo in 319 subjects enrolled in two double-blind, vehicle-controlled studies. Subjects applied up to two packets of ZYCLARA Cream or vehicle daily to the skin of the affected area (either entire face or balding scalp) for two 2-week treatment cycles separated by a 2-week no-treatment period.

Table 1: Selected Adverse Reactions Occurring in ≥2% of ZYCLARA-Treated Subjects and at a Greater Frequency Than With Vehicle in the Combined Studies

Preferred Term	ZYCLARA Cream 3.75% (N=160)	Vehicle (N=159)
Headache	10 (6%)	5 (3%)
Application site pruritus	7 (4%)	1 (<1%)
Fatigue	7 (4%)	0 (0%)
Nausea	6 (3%)	2 (1%)
Application site irritation	5 (3%)	0 (0%)
Application site pain	5 (3%)	0 (0%)
Pyrexia	5 (3%)	0 (0%)
Anorexia	4 (3%)	0 (0%)
Dizziness	4 (3%)	0 (0%)
Herpes simplex	4 (3%)	1 (<1%)
Pain	4 (3%)	0 (0%)
Chest pain	3 (2%)	0 (0%)
Diarrhea	3 (2%)	0 (0%)
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Table 2: Local Skin Reactions in the Treatment Area in ZYCLARA-Treated Subjects as Assessed by the Investigator

	ZYCLARA Cream 3.75% (n=160)		Vehicle (n=159)	
	All Grades*	Severe	All Grades*	Severe
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Endocrine: thyroiditis.

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Respiratory: dyspnea.

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USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Category C:

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Issued: March 2010
ZYC0410135